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Aims and Scope:- JK-Practitioner is a multidisciplinary Medical Journal published quarterly from Srinagar. Emphasis is placed on matters related to medicine in this country in particular, while articles from anywhere in the world are given due importance. Besides original articles and case reports the journal includes clinical reviews, guest articels and special articles on current aspects in medicine and therapeutics.

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FROM THE CHIEF EDITOR

*We are presenting before you the first issue of JK-Practitioner in the new millennium. The journal, the first of its kind in the state was launched in October 1994, and since then has maintained the reqularity in publication originally envisaged-quarterly. The jouranl got indexed with the international agency, **EMBASE/ EXCERPTA MEDICA** in 1995. I have no doubt that, very soon the journal will be indexed in other medical databases.*

During the last 6 years we have been able to knit together an excellent team of consultant editors, advisory board and editorial committee, who are working hard to see the journal attain and maintain international standard and recognition. The Editor's office has been receiving encouraging comments regarding the journal from every corner of the world. We assure our readers that there will be no letup in our efforts to bring, through this journal, authentic, original and useful information at your doorstep.

The journal is now being subscribed by many reputed institutions within the country and abroad. Although financial constrains many slow our march to attain perfection, but we will not allow this to be a stumbling block.

The journal has been sponsoring guest lectures/symposia in Kashmir in collaboration with IMA, GMC, Srinagar/ SKIMS Soura, to serve the purpose of CME in the State - a highly neglected area. Besides this the journal also sponsored awards, medals and cash certificiates to deserving young doctors of the State.

I am greatly thankful to the consultant editors, the advisory board members and all those doctors who have acted as referees/ reviewers for the articles submited for publications to the journal.

I wish a happy new millennium to all the doctors, editorial team and Office Staff

Prof. G.M. Malik
Editor-in-Chief
JK-Practitioner,
Srinagar January 2000

ERRATA

I. Article: **Magroob M et al. Non-Psychiatrit Clinicians Training in Psychiatry, its Perceived Adequacy and Modalities of treatment used. JK-Practitioner 1999;6(4): 273-277**

1. Please read Zaffar Ali DNB as author no. 2 after M.Magroob MD Page 273.
2. Also, Following tables are to be read with the article.

TABLE 1:

Speciality wise break up and socio-demographic characteristics:

Sex:		
	male	58 (81.69%)
	female	13 (18.31%)
Age wise distribution:		
	<30 yrs	8 (11.26%)
	31-40 yrs	15 (21.13%)
	41-50 yrs	31 (43.66%)
	> 51 yrs	17 (23.94%)
Years in clinical practice:		
	< 3 yrs	3 (4.23%)
	3-6 yrs	6 (8.45%)
	7-10 yrs	4 (5.63%)
	> 10 yrs	51 (71.38%)

Specialty wise distribution:

Medicine:	18 (25.35%)	Surgery:	8 (11.27%)
Obs & Gynaecology:	7 (9.86%)	ENT:	8 (11.27%)
Orthopaedics	3 (4.22%)	Pathology:	3 (4.22%)
Anaesthesiology:	3 (4.22%)	Radiology:	2 (2.81%)
Neurology:	1 (1.41%)	Paediatrics:	5 (7.045)
Ophthalmology:	4 (5.63%)	Dentistry:	7 (7.04%)
Anatomy	4 (5.63%)		

Table 2

Modalities of treatment used

Modality used	No. of users (total 71)
1. Reassurance	31 (43%)
2. Tranquilisers	30 (42%)
3 Reassurance with tranquilisers	50 (70%)
4 Counseling	11 (15%)
5 Psychotherapy	12 (16%)
6 Crisis intervention techniques	4 (6%)
7 Referral to the emergency of a general hospital	5 (7%)
8 Referral to a psychiatrist / psychiatric disease hospital	53 (75%)

Table 3

Reasons for referral to a psychiatrist

1 Request from the patient to see a psychiatrist	12 (17%)
2 Patient was excited and unmanageable	30 (42%)
3. Pressure from the relatives of the patient	11 (15%)
4. Serious impairment of the patients working capacity	24 (34%)
5 Pressure from the relatives of the patient	4 (6%)
6. Lack of emotional support from the family	17 (24%)
7. Others	
- to confirm diagnosis and treatment	35 (49%)
- for detailed examination	18 (25%)
- resistant cases	18 (25%)
- time does not permit psychiatric counseling	7 (10%)
- for better management	47 (66%)
- unable to diagnose	19 (27%)

Editorial

NEURAL TUBE DEFECT AND FOLIC ACID

Mohammad Afzal Wani MBBS. MS. Mch. FICS. FIMSA

Neural tube defects (NTD) are defined as a group of cogenital anomalies which include, anencephaly, encephalocele, iniencephaly (cranial defect at the occiput with the brain exposed), meningocele, myelomeningocele, myeloschisis (cleaving of the cord), lipomeningocele and rashischisis (division of the spine). This group does not include cases who have isolated hydrocephalus, hydroencephaly and dermal sinus.

Because of the cyst-like formation Meningocele, myelomeningocele, myeloschesis and lipomeningocele are collectively known as spina bifida cystica. This is the most serious and common form of the disease.

Historical Background:

Spina bifida (SB) was recognized almost 12000 years ago when skeletons with spina bifida were recovered from Morocco. Following extensive anatomical dissection, its present name was first used by Professor N. Tulp. Ruyscn in 1691 sub grouped spina bifida in to the paralytic and non-paralytic varieties. In the nineteenth century various type of defects were recognized and anatomical illustrations were published[1].

Incidence:

From various parts of the world an incidence of 0.1 to 4.5/1000 live births has been reported[2,3]. Cogenital malformations of the CNS constitute more than half of all the cogenital malformations[4,5] with an incidence of 1-2 per 1000 births[5,6]. This is inspite of the fact that at least 50% of defective embryos, having a malformation of the CNS undergo spontaneous abortion or resorption. A majority of these are anaecephalics or have myelomeningoceles. From the Saudi Arabian panenisula an incidence of 0.82 and 1.62/1000 live births has been reported[7,8].

Kashmir Experience:

Approximately 18,000 (17,973) babies were born at a regional Maternity and Child Health Centre in Kashmir valley in one year period. 17,323 were born alive and 650 were still births. Congenital mal formations of the Central Nervous system were ascertained. Thirty eight infants had congenital anomalies of the Central Nervous system. Over all incidence of these anomalies was 2.1 per 1000 births. 650 out of 17,973 were still born. Frequency of CNS defect was high in still born babies 57.99%. While among live born infants it was 0.09% (16/17323). Anencephaly was more common in females. A high percentage of anencephalic infants were still born (98%). The median age at death for live born infants with anencephaly was 10 hours.No anencephalic infants were put on live support. Pregnant mothers from Rural areas, ladies from low socio-economic status and the one's with inadequate prenatal assesment and follow up had higher incidence of CNS malformation.[1a]

Embryology:

The first 60 days of gestation in the human being constitute the embryonic phase of development. Most of the CNS is formed from the outer germ layer, the ectoderm. The notochord develops at 3 weeks. The notochord canalises to form a tube and is in communication with the amnion through the primitive pit. By the end of the third week of gestation, a thickening of the ectoderm, situated on the dorsal surface, constitutes the neural plate. Its centre becomes depressed to form a groove lined on each side by a neural fold and at the same time, somities (lateral mesodermal condensations) begin to appear. The closure process leaves an opening rostrally, the anterior (cranial) neuropore which close around the 25th day of geslation and an opening caudally, the posterior neuropare which closes by 30th day gestation. This explains most of the cogenital anomaliers are located in the cranial and caudal regions. The CNS now appears as a closed tubular structure with a narrow caudal spinal cord and a broader cephalic portion. The basic embryological defect in SBC. (Spina bifida cystica) is failure of the caudal neuropore to close at around 28 days of gestation. Failure of the cranial (anterior) neuropore (anterior to the 4th somite) to close at around 26 days leads to various forms of brain malformation like anencephaly and encephalocele. Aetiology, pathogenesis and the regional variations of SB (Spina bifida) have not been fully established inspite of its discovery centuries ago. Failure of the posterior vertebral arch(es) to fuse at the midline (spina bifida) could occur as an isolated defect which involves one or more vertebra without any clinical significance as in spina bifida occulta, or secondary to the failure of the neural tube to close as in spina bifida cystica.

Genetic, environmental, racial and metabolic causes have been put forward, but none have been proved beyond doubt to be the causative agent. Most probably it is of a multifactorial aetiology with a distinct genetic predisposition[9] Myeloschisis which is the most severe form of SBC (spina bifida cystica) may result from overgrowth of the neural plate in the dorolateral direction and subsequently failure of the caudal neuropore to close[9].

Animal studies by Brook & Straatan using the curly-tail mouse as a model for NTD (Nural tube defect) indicated a disturbance in the balance of the rate of growth between the dorsal and the ventral regions of the neural plate i.e. delayed growth rate of the notochord and the gut. This is caused by temporary block of the posterior neuropore to close due to excessive ventral bending of the neural plate and increased strain on the neuroepithelium and subsequently prevention of the elevation of the neural folds and failure of closure[10]. A decrease in production and delay in degradation of hyaluron (a glycosamingolycan) at the site of maximum proliferation in the region i.e. the notochord and the gut wa demonstrated by the same group in their further studies[11]. Derrangement of homocysteine metabolism has also been implicated as a cause for anomaly of neural tube defect[12]. With these observations the possible pathogenesis of NTD (Neural tube defect) has shifted from a physical factor to a factor at molecular and genetic level. Preventing occurance of Neural tabe defect is the most exciting aspect of this serious congenital malformation which has evolved over the last 20 years. An interest in folic acid in relatin to NTD has been pursued after the observation of Hale (1933)[13]. He emphasised the importance of the nutritional deficiences as a cause in congenital malformation. Hibbard & Smithells published their preliminary report about the relation of folate to human embryopathy in 1965[14].

Neural Tube Defect and Folic acid Supplementation

Prevention of Neural Tube defect by using folic acid supplement in high risk (affected) mothers came to light from two types of studies. Observational work was conducted by[15,16,17,18,19] and International studies was conducted by many people[20,21,22,23,24]. Observational studies depended on either on the history of vitamin uptake before and during pregnancy[15,18] or estimating folate and other vitamin levels of the pregnant women[19]. Some of the observational studies failed to show any signficant benefit from folic acid intake[18,19]. A major flaw of these studies was that these were carried out after the events. Some of the babies with Neural tube defect had a long follow up of almost 15 years[18].

Almost all the international studies mentioned and a few more not cited have shown a significant protective effect of folic acid use. The most important study is the MRC multicentre, randomised double-blind trial which involved 33 centres in seven countries[24]. A total of 1817 high-risk mothers identified, because of a previously affected pregnancy, were stratified into four groups; a) folic acid b) other vitamin with folic acid c) vitamin without folic acid and d) placebo. This study provided definitive evidence of prevention by using folic acid. It showed a 72% protection to a fetus/infants from Neural tube defect in mothers who had previously had an affected baby. There was an occurrence risk of 1% inthe group which received folic acid with or without other vitamins in comparisons with a 3.5% risk in unsupplemented mothers. The dose of folic acid used in this trial was 4 mg daily.

In a recen study Czeizel et al. from Hungary demonstrated a reduction in first occurrence of Neural tube defect in women who were supplemented with multivitamin tablets containing 0.8mg of folic acid (13.3/1000 vx 22.9/1000m p-0.02).[25] The current recommendation of the American Public Health Services is as follows; all women of childbearing age should consume 0.4 mg of folic acid daily inorder to reduce the risk of having pregnancy affected by Neural tube defect. Women who have had previously affected fetus/infant should consult their doctor for advice[26].

Conclusion:

In the developing world and areas where incidence of Neural tube defect is high, a collective effort should be made by obstetricians, paediatricians, neonatologists and family doctors to increase the awareness amongst women in the childbearing age, of the need to take multivitamin tablets which contain at least 0.4 mg of folic acid daily before they became pregnant. By the time the pregnancy test is positive or a woman asks herself 'Am I pregnant' it would be too late. This could also be propagated through various media agencies and T.V. programmes. Health workers are to be advised and instructed to spread this message at village levels. Women who have had a previously affected fetus/infant should be seen in special counselling clinics at 6 to 8 weeks. These women may need a higher dose of folic acid, between 1 and 4 mg daily before and during the first trimester in all subsequent pregnancies.

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What do you need to know about Hepatitis A

Q. What is hepatitis A ?

A. Hepatitis A is one of the most widespread infectious diseases worldwide. It is caused by the hepatitis A virus and is common in places with poor standards of hygiene and sanitation. The virus attacks the liver and causes varying degrees of illness in patients.

Q. How is hepatitis A transmitted?

A. The hepatitis A virus is excreted in the faeces, and spreads primarily by the faecal-oral route. The virus has a relatively long and infectious incubation period. Hence, the infected individual can pass on the disease to others even before the symptoms develop. Hepatitis A in children under 2 years is often unrecognized; thus they can be a potential source of infection. Direct contact with an infected person's faeces or indirect contamination of food, water, hands and cooking utensils may result in the virus being ingested, causing infection.

Q. What are the sources of infection?

A. A common source of infection is contaminated water or food, especially raw or insufficiently cooked food (fruits, salads, vegetables, seafood etc.). Food which is well cooked but handled by infected individuals can also be a source of infection. The infection may also be acquired through close contact with infected individuals within families, schools , daycare centres and hostels.

Q. How serious can hepatitis A infection be ?

A. The severity of infection is age related with symptoms being more common in adolescents & adults than very young children. Acute symptoms last for 4 weeks to 3 months and may be debilitating requiring total rest and occasionally hospitalization. This causes disruption of daily activities and often leads to absence from work / school. Complete recovery can take as long as 6-12 months, with serious and occasionally fatal complications occurring in minority of patients. Hepatitis A can relapse in 20 % of cases who acquire the disease, and the symptoms may persist for upto 6 months.

The negative influence on productivity and quality of life though unmeasured, can be quite high.

Q. What are the symptoms of Hepatitis A?

A. Symptoms include nausea/vomiting, yellowness of eyes, skin & urine (Jaundice), diarrhoea, pale stools, abdominal pain, malaise/ fatigue, fever/chills, lack of appetite, sore throat, etc. The frequency/ severity with which these symptoms occur vary depending on the age of the person.

Q. Does hepatitis A pose a serious threat to the health of young children?

A. Though hepatitis A is considered to be a relatively benign disease in young children, this may not always be the case. Children present with more atypical signs and severe gastrointestinal symptoms than adults. There is evidence to suggest that over 60% of 2-5 year olds develop jaundice with associated dark urine and pale stools. The significant health risk that severe diarrhoea, nausea and vomiting can present to the young should not be forgotten.

Q. Does improvement in living conditions decrease the chances of infection with hepatitis A virus ?

A. Yes, risk of acquiring hepatitis A virus is closely tied to poor standards of living. Poor standards of hygiene and sanitation favor the spread of the virus. Chances of early childhood exposure is high in this setting. In contrast, an improvement in standards of hygiene and sanitation leads to a decline in levels of circulating virus . As a result, risk of early exposure is lesser among those living in an improved socio-economic environment. In this group, contamination is more likely among young children, adolescents and adults.

Q. Who is at risk ?

A. Any non-immune person exposed to the virus can develop hepatitis A. This includes children attending daycare centres, schools, etc. and individuals from upper socio-economic groups who are unlikely to have been exposed to the virus. Travellers to highly endemic areas, food handlers, healthcare workers, school or daycare employees and contacts of infected persons are also at risk.

Q. Can hepatitis A be prevented?

A. Immunoglobulins can be administered to provide temporary protection for 3-5 months. Since regular injections are required to maintain protection, this option is expensive.

A vaccine is now available and is the most practical means of protection against hepatitis A. Primary vaccination protects the person for up to one year and a booster dose administered after 6 months , provides predicted protection for at least 20 years.

Q. If I've been vaccinated against hepatitis B, am I also protected against hepatitis A?

A. No. Each type of hepatitis is different. Vaccination against hepatitis B does not protect from hepatitis A, and vice-versa.

Protect yourself & your family against hepatitis A.
Consult your doctor for more information.

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VIRAL HEPATITIS A TO G & BEYOND….. A PERSONAL PERSPECTIVE

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Viral hepatitis is a national health problem in India. The disease is a major health problem in Kashmir. The valley has been devastated by a number of epidemics of hepatitis in recent years and the disease is endemic in the state. It was in 1978 that the author described a new viral hepatitis from an epidemic of jaundice, which occurred in Tangmarg, Baramulla and Sopore. The disease was water-borne and caused by gross fecal contamination of Ningli Nallah, which flows from Gulmarg valley into Wullar Lake. The disease was named as Epidemic non-A, non-B hepatitis and latter renamed as hepatitis E. Hepatitis E Virus (HEV) – the etiological agent of hepatitis E – is one of the 5 major pathogens in the viral hepatitis family and causes epidemics and sporadic acute viral hepatitis in developing countries.

The manuscript to follow is a personal perspective of the author of the present knowledge of viral hepatitis, trends in it's management and future progress likely to occur as we enter the next millenium. At the end I have listed a number of key references from where further information could be obtained, should readers choose to do so . Following that I have listed another 25 references which have been published in the field of viral hepatitis by me and my colleagues over the years. These references have found place in top ranking international journals and have brought Kashmir on international scene in the field of medical research.

Viral hepatitis is a cause of considerable morbidity and mortality, both from acute infection and the chronic sequelae. It is a global health problem and breaks all known human barriers in causing disease and suffering. Globally over 850 million are chronic carriers of hepatitis viruses B and C and account for over 2 million deaths per year. During the last 20 years, there has been a dramatic improvement in the understanding of viral hepatitis, the consequences of which will affect hundreds of millions of people throughout the world. Inspite of these developments, viral hepatitis shall continue to be a major health problem to mankind for many years to come.

Definition

By definition viral hepatitis is an infection caused by a group of hepatotropic viruses, known and unknown. By hepatotropism we mean that the agent should have a special affinity for or exerting a specific affect on the liver. Other agents such as cytomegalovirus and Epstein-Barr virus also cause hepatitis but as a part of a systemic infection in which liver is only one of the several organs or systems affected. These agents are therefore not included in the list of hepatitis viruses.

It is now recognized that five unrelated human viruses cause most cases of viral hepatitis (table 1). Hepatitis A virus (HAV) and hepatitis E virus (HEV) cause infectious or epidemic hepatitis and are transmitted by the feco-oral route. HEV is also responsible for high mortality in pregnant women. Hepatitis B virus (HBV) and the recently identified hepatitis C virus (HCV) are spread by various non-enteric routes and are endemic or hyperendemic in most human populations. Both are associated with chronic hepatic disease and also with primary liver cancer. Hepatitis D virus (HDV) characteristically co-infects or superinfects patients with hepatitis B and it is an important cause of severe chronic liver damage in HBV carriers.

Discovery

Of the agents, five well-defined viruses A to E are of major clinical importance. The discovery of these viruses has followed a generally uniform pattern namely description of disease, animal transmission, visualization of virus by immune electron microscopy and subsequent cloning and sequencing of the virus. The human transmission experiments of Saul Krugman et al at the Willowbrook State school in New York, an institution for the mentally retarded, distinguished infectious and serum hepatitis and led subsequently to identification of HAV and HBV. Alter et al from NIH Betheseda described non-A, non-B hepatitis in multiply transfused open heart surgery patients which led to animal transmission and subsequent cloning of hepatitis C virus.

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Our group described epidemic non-A, non-B hepatitis, which set pace for human and animal transmission and subsequent cloning of HEV. Rizetto et al from Italy identified and recognized the delta virus as a major factor influencing the severity of chronic hepatitis B infection. HDV was subsequently propagated in chimpanzees, cloned and sequenced.

Table 1: Five major pathogens of viral hepatitis, their genomes and clinical consequences

Agent	Genome	Clinical Consequences
Enteric		
HAV,Piconavirus, 27 nm	4.5 kb, ssRNA	AH, FHF
HEV, Calcivirus 32 nm	7.5 kb, ssRNA (+)	AH, FHF
Parenteral		
HBV, hepadnavirus, 42 nm	3.2 kb, dsDNA	AH, FHF, CH^b, Cirrhosis, HCC
HCV, Flavivirus 30-60 nm	9.4 kb, ssRNA	AH, Cho, Cirrhosis, HCC
HDV, Satellite, 35-40 nm HCC	1.7 kb, ssRNA (-)	AH, FHF, CHd, Cirrhosis

AH = acute hepatitis; FHF = fulminant hepatic failure; CH = chronic hepatitis, HCC = hepatocellular carcinoma; a = > 20% in pregnant women; b = 5% in adults and > 90% in neonates; c = 50-80%; d = 5% in coinfection and > 50% in superinfection.

Epidemiology

WEST: Do these 5 agents accounts for all major clinical consequences of viral hepatitis (table 2)? In the United States, around 300,000 cases of acute viral hepatitis are reported per year. The major pathogens causing this syndrome are HAV, HBV and HCV. Only 2% of such infections are of unexplained etiology. Acute liver failure is a dramatic and challenging syndrome with high mortality. It is characterized by occurrence of encephalopathy and coagulopathy with underlying massive hepatic necrosis. Around 2000 cases of acute liver failure occur in USA per year. HAV and HBV cause around half of cases of acute liver failure, while the other half are caused by yet unknown viral agent / agents. Chronic viral hepatitis constitutes 75% cases of cirrhosis and major known causes are HCV and HBV. In this group around one third of cases are cryptogenic and presumably caused by yet unknown viral agent.

East In contract epidemiology of viral hepatitis in developing countries is different. Acute viral hepatitis is rampant and a major cause of morbidity and loss of working days in young adults. HEV is the major pathogen causing around half of these cases. In addition to sporadic acute viral hepatitis, massive water borne epidemics involving hundred of thousands of patients are exclusively caused by HEV. Acute liver failure in developing countries is much more common especially occurring during pregnancy and also caused exclusively by HEV. Around 25% to 40% patients with acute viral hepatitis and acute liver failure are caused by yet unknown viral agent /agents.

Thus, the list of viral agents causing various clinical syndromes of viral hepatitis is incomplete with around half of clinical cases caused by agents yet unidentified. In view of this, massive research projects are on world over to identify new viral agents from appropriate clinical material.

Table 2: The agents implicated in causing various syndromes of viral hepatitis in Western Europe and the USA (West) and the Indian subcontinent and other developing countries (East)

	Disease (%)					
Agent	AVH		ALF		CVH	
	West	East	West	East	West	East
HAV	40	4	17	3	-	-
HEV	-	40	-	37	-	-
HBV	30	22	27	18	25	25
HCV	25	9	-	5	45	45
N-A-E	2	25	55	37	30	30

AVH = acute viral hepatitis, ALF = acute liver failure, CH = chronic hepatitis, N-A-E = non-A, non-B hepatitis

Hepatitis A Virus

Hepatitis A virus (HAV) is an enteric pathogen with high person to person transmission. In developing countries, HAV exposure occurs early in life, with subsequent life long immunity. In countries with improved hygiene and sanitation, hepatitis A in children is unusual, thus adults in such countries are susceptible to HAV. There is recent significant increase in reported hepatitis A under certain epidemiological situations in USA namely travel to developing countries especially Indian subcontinent and Africa, day care centres and following ingestion of shellfish. In addition, cyclical hepatitis A epidemics have been reported in a number of counties in USA over last 2 decades. Hepatitis A in adults is more often icteric and has higher morbidity and mortality.

In addition to higher mortality, a number of clinical syndromes of hepatitis A have been reported in adults in USA. These include protracted hepatitis lasting for 3-6 months, cholestatic hepatitis resembling extra-hepatic biliary obstruction and multiple relapses of hepatitis superficially resembling and to be differentiated from chronic viral hepatitis.

Hepatitis E Virus

Hepatitis E virus (HEV) is recent introduction to hepatitis viruses family. The agent has a particle size of 32-34 nm with spikes and indentations on its surface. The genome has a single positive stranded polyadenated RNA of approximately 7.5 KB. Three ORF's have been postulated so far. The virus belongs to a group of Calciviridae or a new class of alpha viruses.

HEV is an enteric pathogen superficially resembling HAV. However, person to person contact does not transmit HEV and attack rate is high in adults with very low attack rate in children. The disease presents as large-scale water borne epidemics involving hundreds of thousands of people. These epidemics cause national health problem in such countries. One of the most distinguishing features of HEV infection is its increased incidence and severity in pregnant women. The mortality of HEV infection in pregnant women is around 20% as against less than 1% in men and non-pregnant women. The reason for this is unknown and is possibly related to biological behavior of the infectious agent. Very early we recognized the relationship of HEV with animal Kingdom and proposed that it may be a zoonotic disease. Subsequently, HEV antibodies were detected in a wide range of animal Kingdom especially rheusus monkeys, cattle and swine.

As hepatitis E is ecologically determined disease, its control shall be finally brought up by supply of pure portable water supplies in such regions. Studies of passive immunoglobulin from endemic areas have been done but have not proved of value in reducing death rate in pregnant women during epidemics.

As HEV is a stable virus, vaccine production has been not very difficult. Already 2 vaccines have been shown to give protective antibodies in monkeys and in near future, may be used in clinical setting. The 2 vaccines are recombinant baculovirus 5a Kda truncated protein and ORF2 subunit protein.

Table 3: Chronic Hepatitis B Infection
Stages of Infection

			HBV DNA		
Stage	ALT	e antigen	Dot Blot	PCR	Histology
Tolerance	N	+	++	+	Inactive CPH
Cytolysis	(((	+	++	+	CAH/CLH/CH
Seroconversion	N	-	-	+	Inactive (CPH/CH)
Mutant	(((	-	++	+	CAH/CLH, Active Cirrhosis HCC

N = normal, (((= elevated, + = detected, ++ = detected in large amounts, - = not detected, CPH = chronic persistent hepatitis, CAH = chronic active hepatitis, CH = cirrhosis, CLH = chronic lobular hepatitis, HCC = hepatocellular carcinoma

Hepatitis B Virus

Hepatitis B virus (HBV) is a human pathogen of great importance mainly from its behaviour to cause chronic liver disease. The distribution of HBV infection varies greatly throughout the world. In high endemic zones, with a carrier rate of over 8% and population exposure rate of over 80%, the virus is mainly spread by perinatal transmission. Such infections are subclinical with chronicity of over 90%. In intermediate endemic zones with carrier rate of 3-8%, horizontal transmission occurs from one child to another especially in preschool and early school life. Such infections are also subclinical with chronicity of around 30%. In low endemic zones a small fraction of population is exposed to the virus in adult life through parenteral or sexual route. Such infections carry chronicity rate of around 5%.

Life cycle of HBV in the human host has undergone conceptual change. Understanding this has become essential to organize antiviral therapy in patients with HBV. Broadly it is useful to consider the life cycle of HBV into four stages in all infected patients (table 3). The first stage is characterized by host immune tolerance. Active viral replication occurs with high serum HBV DNA load and HBeAg, little or no elevation of aminotransferase, minimal hepatitis and no clinical symptoms. This stage lasts for decades in neonatal infections in endemic zones and has earlier been identified as healthy HBV carriers.

During stage of cytolysis, host immune mechanism leads to attempt at virus clearance, causing cell lysis and a hepatic inflammatory process. HBV DNA levels and HBeAg is detectable in low titres, aminotransferase levels are elevated, liver biopsy reveals lobular and portal hepatitis and recurrent or continuous clinical symptoms occur. This stage lasts for 10 or more years and is the stage where chronic liver disease - chronic hepatitis and cirrhosis develop.

In the third stage of sero-conversion, active viral replication ends, HBV DNA levels are extremely low (detectable only by PCR) and HBeAg is no longer present and antibody to HBeAg becomes detectable. Enzyme levels are normal and liver biopsy lacks inflammation and cytolysis, but may show underlying normal histology to established cirrhosis.

During the fourth stage, patients clear HBsAg and antibody to HBsAg appears, and patients are no more infected. However, in the Mediterranean region and far east, a group of patients during this stage undergo escape mutation, have high HBV DNA titres, secrete no HBeAg, have high serum enzymes and marked lobular and portal inflammation. Around one third of chronic HBV in these countries are related to mutant HBV - either caused by denovo infection or a result of escape mutation. Patients with chronic HBV with HBeAg minus viremia are associated with considerable HBV induced liver disease and an unfavourable prognosis.

While planning interferon therapy, it is important to find that patients are in the clinical phase of cytolysis and the drug accentuates the immunological reaction of the host to eliminate the virus.

Hepatitis D Virus

Hepatitis D virus (HDV), initially termed "delta agent" and then "hepatitis delta virus," is a defective RNA-containing virus that requires the helper function of the hepadnaviruses for its expression and pathogenicity. Both HDV/HBV coinfection and HDV superinfection can lead to the clinical picture of typical acute hepatitis, fulminant hepatitis, or chronic hepatitis. Because most HBV infections in adults are short-lived, and because HDV infection cannot persist after recovery from HBV, the majority of coinfections are self-limited although fulminant hepatitis is a well-known complication. In contrast, HDV superinfection can cause fulminant hepatitis and rapidly progressive chronic hepatitis.

Hepatitis C Virus

Hepatitis C virus (HCV) is widely distributed around the world with a prevalence of infection of 0.1-0.2% in the west, 3% in Mediterranean countries and 6% in tropical areas. It has become increasingly clear in recent years that hepatitis C, once thought to be a benign disease, is considerably more important than hepatitis B. Hepatitis C accounts for two thirds of the deaths from chronic liver disease, is leading cause of liver transplantation and has higher propensity to progress to HCC than HBV. Around 90% of all liver cancers in Japan are related to HCV.

One of the remarkable features of HCV is its natural history in the host. Acute HCV infection is symptomatic in around 35% of individuals - usually these symptoms are mild and non-specific. However, 85% - 100% of patients are unable to clear the virus, inspite of the antibody response mounted against the virus. Of the patients with persistent infection, 50-70% develop evidence of chronic hepatitis. The course of chronic HCV infection is highly variable and rate of progression in individual patients is unpredictable. At least 20% of patients would progress to cirrhosis in 20 years and another 20% would develop hepatocellular carcinoma.

Clinical course of HCV is usually associated with episodic fluctuations of serum aminotransferases reflecting waves of hepatocellular inflammation and necrosis. Such episodes may be related to emergence of HCV neutralization escape mutants. In fact heterogenicity in HCV genome is important features and sequence variation of the genome occurs mainly in NS2, E1 and E2 regions with high degree of conservation in non-coding C, NS3, NS4 and NS5 regions.

Currently available therapy for chronic hepatitis C is indicated for patients who have persistently abnormal aminotransferase levels (>6 months), a positive HCV RNA, and liver biopsy specimen demonstrating either portal or bridging fibrosis and at least moderate degrees of inflammation and necrosis. Patients with milder histological disease, compensated cirrhosis, or who are younger than 18 or older than 60 years should be managed on an individual basis or in the context of clinical trials. Patients with decompensated cirrhosis should not be treated with interferon, but should be considered for liver transplantation. Patients with persistently normal aminotransferase levels and minimal histological abnormalities should not be treated outside of clinical trials.

Interferon

Interferon therapy of chronic viral hepatitis has been studied over a number of years; different interferon preparation, doses and schedules have been used. Meta analysis of these studies shows that sustained response rate in chronic hepatitis B approaches 35 to 40%, while sustained response rate in chronic hepatitis C is at best 15-20%. Chronic HDV infection is least likely to demonstrate sustained response. These response rates are limited to a highly selected group of patients with chronic viral hepatitis and it is obvious that the treatment of these infections with interferon is not optimum. This has led to exploring alternative treatment options for these infections.

Ribavirin

In terms of biochemical response, treatment with interferon alpha in chronic HCV at a dosage of 3 million units administered subcutaneously three times weekly for 6 months has produced a biochemical end of treatment response of 40% to 50% and a biochemical sustained response of 15% to 20%. In terms of virological response, the 6-month course of treatment has produced an end of treatment response in 30% to 40% and a sustained response in 10% to 20%. The biochemical and virological improvement has been accompanied by histological improvement.

At present, the adjunctive drug of most promise is ribavirin, an oral antiviral agent that, when used alone, reduces serum aminotransferase levels in approximately 50% of patients. However, ribavirin by itself does not lower serum HCV RNA levels and relapses occur in virtually all patients when therapy is stopped. Of greater promise are recent reports that the combination of interferon alpha and ribavirin leads to higher virological sustained response rates (40% to 50%) than interferon alpha alone in 6-month clinical trials. The Food and Drug Administration (FDA) USA have licensed ribavirin for use in hepatitis C. Combination therapy with ribavirin and interferon has also shown promise in the re-treatment of patients who relapse. Hemolytic anemia has been the major side effect of ribavirin, necessitating a dosage reduction in one out of 10 patients.

Lamuvidine

Nucleoside analogue namely Lamuvidine and Famclovir have been shown to possess antiviral property against HBV. Lamuvidine, an enantiomer of 3'-thiacytidien, inhibits HIV replication and has antiviral activity against HBV, with less toxicity than its predecessor, zalcitabine. Lamuvidine administered for 4-12 weeks in patients with HBV infection demonstrated the clearance of HBV DNA from serum during treatment in 100% of patients but sustained remissions in only 20% of patients. One year trials have led to similar results. The recurrence of viremia after cessation of therapy is likely. With prolonged treatment escape mutants develop in around 16% of patients at one year.

Liver transplant recipients appear to benefit from lamuvidine. In a small study, treatment with 100mg of lamuvidine daily resulted in clearance of HBV DNA and HBsAg after one year in 90 percent of patients, when treatment was begun before transplantation. It is likely that treatment with nucleoside analogues will have to be maintained indefinitely, at least in immunosuppressed patients; prolonged treatment is probably feasible, since the side effects appear to be minimal.

Hepatitis B Vaccine

Prevention of HBV infection by vaccination is the ideal and most economical approach. In 1991, the Global Advisory Group of EPI recommended that all countries irrespective of their endemicity status should introduce hepatitis B vaccine into their National Vaccination Program. In fact around 80 countries worldwide have introduced the vaccine into EPI program. The impact of immunization on hepatitis B epidemiology in these countries has exceeded the expectations and children cohorts immunized have shown marked reduction in carrier rate and in occurrence of chronic liver disease and hepatocellular carcinoma. Currently, the most commonly used vaccines are composed of HbsAg, produced by two different methods namely plasma-derived and recombinant DNA technology. When properly administered, such vaccines provide protection in about 95 percent of recipients.

Hepatitis A Vaccine

Hepatitis A vaccine is a formaline-inactivated alum-adsorbed whole-virion vaccine. It is currently distributed in about 50 countries. Extensive experience with use of this vaccine has shown that it is safe, well tolerated and highly effective. As of today vaccine has been used in following situations: a) in presumed non-immune business and leisure travelers to developing countries, b) in Armed Forces, among close contacts of cases and in at risk occupational groups, c) to interrupt community-wide hepatitis A outbreaks. So far no country has developed a national policy to use the vaccine in a systematic immunization program to control infection in the general population. Availability of combined hepatitis A and hepatitis B vaccine would facilitate the acceptance and implementation of such a program.

New viral agents

Three new viral agents have been recently cloned and sequenced. The introduction of these 3 agents has followed a different sequence than discovery of major pathogens A to E. A powerful molecular biology tool, namely representational difference analysis, is used to identify new nucleic acids from suspected specimens. None of these agents have been yet implicated in causing any major clinical syndromes of viral hepatitis.

Hepatitis G Virus In 1995-96, the hepatitis G virus (HGV) was cloned and sequenced. This virus is from the group of new agents called GB viruses (GB virus A, GB virus B and GB virus C) and is also designated as GB virus C (GBV-C). HGV is a positive-stranded RNA virus, with a genome of 10 KB and appears, on the basis of genome length and organization, to be a member of the Flaviviridae, distinct from the hepatitis C virus (HCV). HGV infection appears to be transmitted following receipt of blood from HGV RNA-positive donors; however, these patients had only moderate liver enzyme elevations. The strength of the association of HGV infection with acute hepatitis is unclear. Persons infected with the virus appear to remain persistently infected (HGV RNA-positive) for as long as nine years. Although the virus RNA can be detected with varying frequency in patients with various forms of chronic liver disease, an association of the infection with disease has not been demonstrated.

HGV/GBV-C is detected in about 1% of volunteer blood donors with normal aminotransferase values and in approximately 4% of blood donors with elevated aminotransferase values. This data illustrates that the virus is present in the blood supply. It is detected in

15% of intravenous drug users, suggesting a parenteral route of transmission. HGV/GBV-C can be detected in 13% of paid plasma donors. Potentially, the virus is being transmitted through the use of contaminated blood and blood products. Approximately 20% of those individuals with acute or chronic hepatitis C virus infection are HGV/GBV-C RNA positive. The virus establishes a persistent viremia in many individuals, with viral RNA being detected for a year after infection. The virus is detected in only 7% of non-A-E hepatitis cases, including cases of fulminant hepatitis and hepatocellular carcinoma. Eighteen percent of random population from West Africa are positive for HGV/GBV-C. This region is endemic for HBV.

Swine Hepatitis E Virus-Recently studies of HEV in animal Kingdom took an interesting turn by discovery of a novel agent in swine. This agent is closely related but distinct from HEV. The agent has been designated as swine HEV. This agent is ubiquitous in swine and most of piglets have natural infection by 3 months of age. The antibodies to swine HEV cross react with human HEV. Studies in rest of animal Kingdom shall be awaited with great interest. This discovery can have a major impact in vaccine production, diagnosis and biology of this class of viral agents. Whether swine HEV can cause human infection shall also be of interest.

TT-Virus Shunji Mishiro (Toshiba General Hospital) described the discovery of a new DNA virus (TT virus) that is detectable by polymerase chain reaction in 50% of patients with non-AG acute and chronic liver disease. TTV DNA is also present in 12% of volunteer blood donors, complicating analysis of its etiological role in the pathogenesis of non-A-G hepatitis. As a high degree of sequence diversity has been demonstrated among different TTV strains, pathogenic and nonpathogenic genotypes of TTV may exist. Future studies in chimpanzees will hopefully clarify whether TTV is indeed a hepatitis virus.

TTV infection was present in 1% (1 of 100) of blood donors, 15% (5 of 33) of patients with cryptogenic cirrhosis, 27% (3 of 11) of patients with idiopathic fulminant hepatic failure, 18% (2 of 11) of patients with a history of exposure to blood products and 4% (1 of 25) of patients without parental risk factors. For all patients tested, a history of prior exposure to blood products was associated with an increased risk of TTV infection (relative risk, 4.5; 90% confidence intervals 9.6-43.9). Further studies are required to determine the role of TTV in the pathogenicity of acute and/or chronic liver disease.

Putative agents

The story does not end here. Hepatitis F and a paromyxoma like agent have been described to cause acute liver failure in UK and syncetial giant cell hepatitis in Canada respectively. However, these agents have not been cloned and as of today, their identification needs further studies.

Syncetial giant cell hepatitis-Syncetial giant cell hepatitis is a sporadic form of human hepatitis characterized by clinical findings of subacute or chronic hepatitis of greater than average severity, or of fulminant hepatitis; distinctive histopathology of the liver; negative tests for known hepatitis viruses; and the demonstration of paromyxoviral neuclocapsid-like structures within the giant cells on electron microscopy. The hallmark of the disease in liver biopsies is the transformation of the liver cords into fused syncytial giant liver cells. The disease is rare and was first described by Phillips et al from Canada. Following the first description of ten patients in 1991, another 35 patients have been reported worldwide.

Hepatitis F Virus One of the most intriguing aspect of hepatitis epidemiology is defining cause of acute liver failure. Majority of cases of acute liver failure lack markers of all known hepatitis viruses and the predominant cause is an as yet uncharacterized virus. Fagan and co-workers have described toga virus-like particles in hepatectomy specimens of seven of 18 patients engrafted for acute liver failure. All these patients had been negative for known viral etiology. The significance of these findings to the overall etiology of acute liver failure of non-A-E group is unclear.

Hepatitis associated aplastic anaemia. The association between aplastic anaemia and viral hepatitis has been well documented. In Japan, where both hepatitis and aplastic anaemia are more common than in the West, hepatitis has been associated with aplastic anaemia in around 8% of patients. In hepatitis associated aplastic anaemia evaluation rarely reveals presence of HAV and HBV and most cases have been classified as non-A, non-B hepatitis based on serologic exclusion. Pol and co-workers compared 19 such patients to 23 patients of aplastic anaemia of other or unknown etiology; anti HCV and HCV RNA by PCR was detected in 16% and 21% respectively in patients with hepatitis associated aplastic anaemia and 35% and 26% respectively in aplasia of other etiology.

Hibbs et al studied 28 patients with hepatitis associated aplastic anaemia from the USA, Asia and Europe. HCV RNA was detected by PCR in 36% of patients, however, the viraemia appeared to be associated with blood transfusions received after the development of aplastic anaemia rather than being causally related to the development of the aplastic anaemia. Hence, the syndrome of hepatitis associated aplastic anaemia generally cannot be attributed to HAV, HBV or HCV, strongly suggesting the existence of an additional novel agent causing the syndrome.

Waterborne epidemic hepatitis. Waterborne epidemics of hepatitis occur in the developing countries, involving hundreds and thousands of people. The disease occurs in adult population, with high mortality rate in pregnant women. The illness is acute self limiting hepatitis with no evidence of chronic carrier state or chronic liver disease. HEV is the etiologic cause of majority of these epidemics. Over the last few decades since these epidemics are being regularly tested for HEV, over 30 epidemics were studied and found to be serologically related to HEV. However, recently 2 epidemics of presumed waterborne epidemics have been reported in the Indian subcontinent which lacked acute markers of HEV. There was no clinical or epidemiological evidence of exposure to any hepatotoxin in such population. It is strongly suspected that such epidemics were caused by another as yet uncharacterized agent.

In the absence of any solid information regarding the nature of the causative agent(s) of non A-E hepatitis, all molecular "roads" remained open. Primate transmission studies suggested that as many as three separate non A-E viruses might be responsible for the viral hepatitis unrelated to known agents. In fact, application of such molecular approach to presumed non A-E hepatitis led to the discovery of hepatitis G virus (HGV).

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CHILDHOOD TUBERCULOSIS (PART-I) EPIDEMIOLOGY, PATHOGENESIS, CLINICAL PROFILE

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"Tuberculosis is a chronic bacterial infection caused by *Mycobacterium tuberculosis* characterized by formation of granulomas in infected tissues and by cell mediated hypersensitivity". The disease remains a major cause of morbidity and mortality throughout world and is the commonest cause of death from a single infectious disease. The disease was declared a global emergency by WHO in 1993.

Epidemiology: Since children are infected from adults with chronic pulmonary tuberculosis, the extent of infection or disease in children is directly related to prevalence of chronic pulmonary tuberculosis in adults. Prevalence of active disease in adults in India is about 18% annd one-fourth of these cases are bacillary cases in whom sputum is positive. For an estimated population of 950 million in 1997 in India, there would be about 18-20 million active cases of pulmonary tuberculosis, of which 4-5 million would be sputum positive infectious cases. Annual rate of infection (ARI) is 2.1% per year under the age of 5 years[1].

Nearly 40 million children are likely to be exposed to risk and nearly 3-4 million children under 5 years are estimated to be infected and may progress to disease. The younger a child is, there is more risk of developing active disease after primary infection. As many as 43% of children less than one year of age, 24% of children between 1-5 years of age and 15% of adolescents develop tuberculosis at sometime after infection[2]. The ARI in India is 20-25 times higher than in developed countries[3].

The mortality is highest in children below five years of age due to high incidence of severe forms of tuberculosis such as meningeal or disseminated disease. Tuberculosis causes 10-15% of all paediatric deaths in children below 15 years in various Indian hospitals[4]. In a short study, conducted at Govt. Children Hospital, Srinagar during 1997-98, the incidence of tuberculosis was observed to be 4.19% and the disease accounted for 3% of all deaths. In two earlier studies (1977-78 below 5 years age group and 1980 from 0-14 years age group)[5,6] the same was observed to be 4.03% and 7.15% respectively - Table (1) [Unpublished data].

Table - 1(A) Profile of Tuberculosis at Govt. Hospital for Children, Sgr.

Parameter	1977-78 (< 5 years)	1980 (0-14 years)	1997-98 (0-14 years)
Total Hospital admissions	3970	5072	16168
Tuberculosis (TB) (Tuberculosis cases)	160	363	678
Hospital based incidence	4.03%	7.15%	4.19%
Mortality among TB cases	18.72%	NG*	2%

**NG (Not given)*

Table - 1(B) Profile of Tuberculosis in Children Admitted at Govt. Children Hospital, Sgr. (1997-98)

- Total admissions 16168
- No. of tuberculosis Patients 678 (4.19%)

Type of Tubercular Lesion	Number	Percentage
1. Pumonary		
a. Primary complex	110	16
b. Bronchopneumonia	98	14
c. Collapse Consolidation	39	6
d. Miliary	17	4
e. Disseminated	39	6
Total	**303**	**46**
2. Extrapulmonary		
a. Meningitis	221	32
b. Abdominal	77	11
c. Adenitis	47	7
d. Pericarditis with effusion	16	2
e. Bone	14	2
Total	**375**	**54**
Mortality		
Tubercular Meningitis (TBM)	10	2.23
Miliary and other forms	3	0.67
Total	**13**	**3.00**
(2% among tuberculosis patients)		

***Note:** Tubercular meningitis is very high (32%). In an earlier study (1980) in the same hospital, TBM comprised 13.77% of all tuberculosis cases. In the above study, (i.e. 97-98) only 15 patients had a BCG scar with 17 having history of immunization and 86% being unimmunized.*

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Predisposing Factors:

1. Low socioeconomic status, adults with chronic pulmonary tuberculosis, overcrowding, close contact with sputum positive cases, poverty and poverty related diseases etc.
2. Infections like measles, whooping cough, chronic diarrhea and severe malnutrition which lead to T - lymphocyte deficiency and compromised immune mechaenisms, thus activating and precipitating tuberculosis.
3. Drugs like steroids activate otherwise silent and latent tuberculosis and may produce a more disseminated disease.
4. Age: The age below 5 and above- 14 years is the most vulnerable period. Age between 5 - 14 years is often called as the favoured age group, having the lowest incidence of tuberculosis[4].

Pathogenesis: The pathogenesis of primary pulmonary tuberculosis can be described under four stages.

Stage 1: Aerosolised particles containing 1-3 bacilli reach alveoli of lungs, where they are engulfed by macrophages. Mycobacteria may survive or die in macrophages depending on host response. This stage lasts 0-7 days.

State II: In case mycobacteria survive in macrophages, they go into the stage of logarithmic growth lasting upto 20 days.

Stage III: Cell mediated immunity (CMI) and delayed type hypersensitivity (DTH) reaction come into play. In an individual with high level of resistance CMI is good, thus multiplication of bacilli is less which reduces the antigen load. In such individuals tissue necrosis is minimal and the disease does not manifest clinically. The mycobacteria are either eradicated completely or may remain in dormant phase. In cases where CMI is poor, bacillary multiplication is more. In such individuals DTH reaction occurs, causing massive necrosis and clinical manifestations. This stage lasts upto 8 weeks.

Stage IV: In this stage DTH and hydrolytic enzymes cause liquefaction of necrotic tissue. The liquified material is a good growth medium for mycobacteria and this leads to massive extracellular multiplication resulting in cavitation, bronchogenic spread and sysemic dissemination of the disease[7].

Clinical Classification: Childhood tuberculosis is classified as under:

1. **Asymptomatic Mantoux Positive:** 6-8 weeks after infection, Mantoux test becomes positive. If resistance is strong, there are no symptoms. Such patients are detected during family survey.
2. **Symptomatic Mantoux Positive:** Hypersensitivity phenomena, as phlyctenular conjuctivitis, fever and erythema nodosum occur along with Mantoux positivity. There may also be anorexia, listlessness and weight loss of insidious onset.
3. **Primary Pulmonary Complex:** Bacteria after lodging in alveoli set up a primary lesion (Gohn's focus), from where hilar nodes are involved via lymphatics (Primary pulmonary complex of Ranke).
4. **Progressive Pulmonary Disease:** The hilar lymphynodes can press upon bronchus and occlude it partially (Lobar emphysema) or completely (Collapse of lobe). The granulomatous tissue can infiltrate through the bronchial wall and can be aspirated into the alveoli leading to consolidation or bronchopneumonia, if spread is through many bronchi. The consolidation may breakdown and lead to cavitation. From subpleural space, the granuloma can spread to pleura, causing exudative pleural effusion.
5. **Disseminated Tuberculosis:** From hilar nodes, the bacilli can spread into blood stream and lodge in different parts of body leading to disseminated tuberculosis like tubercular meningitis, tuberculomas, tuberculosis of kidneys or bones etc. Hematogenous spread, producing granulomas of same size resembling millet seeds in different organs is called miliary tuberculosis.
6. **Cervical and abdominal tuberculosis:** From the pharynx, the tubercle bacilli can spread to lymphnodes in neck, while from gut the bacilli can extend to mesentric lymphnodes. The other abdominal organs as liver, spleen, retroperitoneal nodes and peritoneum can be involved by hematogenous or local spread.
7. **Tubercular meningitis:** Solitary or multiple metastatic foci in CNS may occur during primary tubercular infection (Riches focus). This may involve meninges, cerebral hemispheres and or spinal cord. When meninges are involved, manifestations can be divided into three stages.
    a. Prodrome: There is non-specific symptomatology.
    b. Appearance of neurological signs and symptoms.
    c. Alteration in level of consciousness.
8. **Progressive BCG disease (BCGiosis):** BCG may

result in non-healing ulcer or abscess and sometimes lymphadenopathy in axillary, supraclavicular or cervical group of nodes. Rarely there may be generalized illness in immunocopromised hosts.

9. **Congenital tuberculosis:** Although rare, as tuberculosis leads to infertility, maternal illness may be transmitted to baby transplacentally by aspiration or ingestion of amniotic fluid if tubercular amnionitis is present. The signs and symptoms appear within 2 months, of life. The clinical features include respiratory distress, hepatosplenomegaly, failure to thrive, jaundice, fever, meningitis and skin lesions[7].

Symptom complexes of tuberculosis[9]: Suspicion is the first and most important step to the recognition of tuberculosis. The symptom complex which arouse suspicion are:

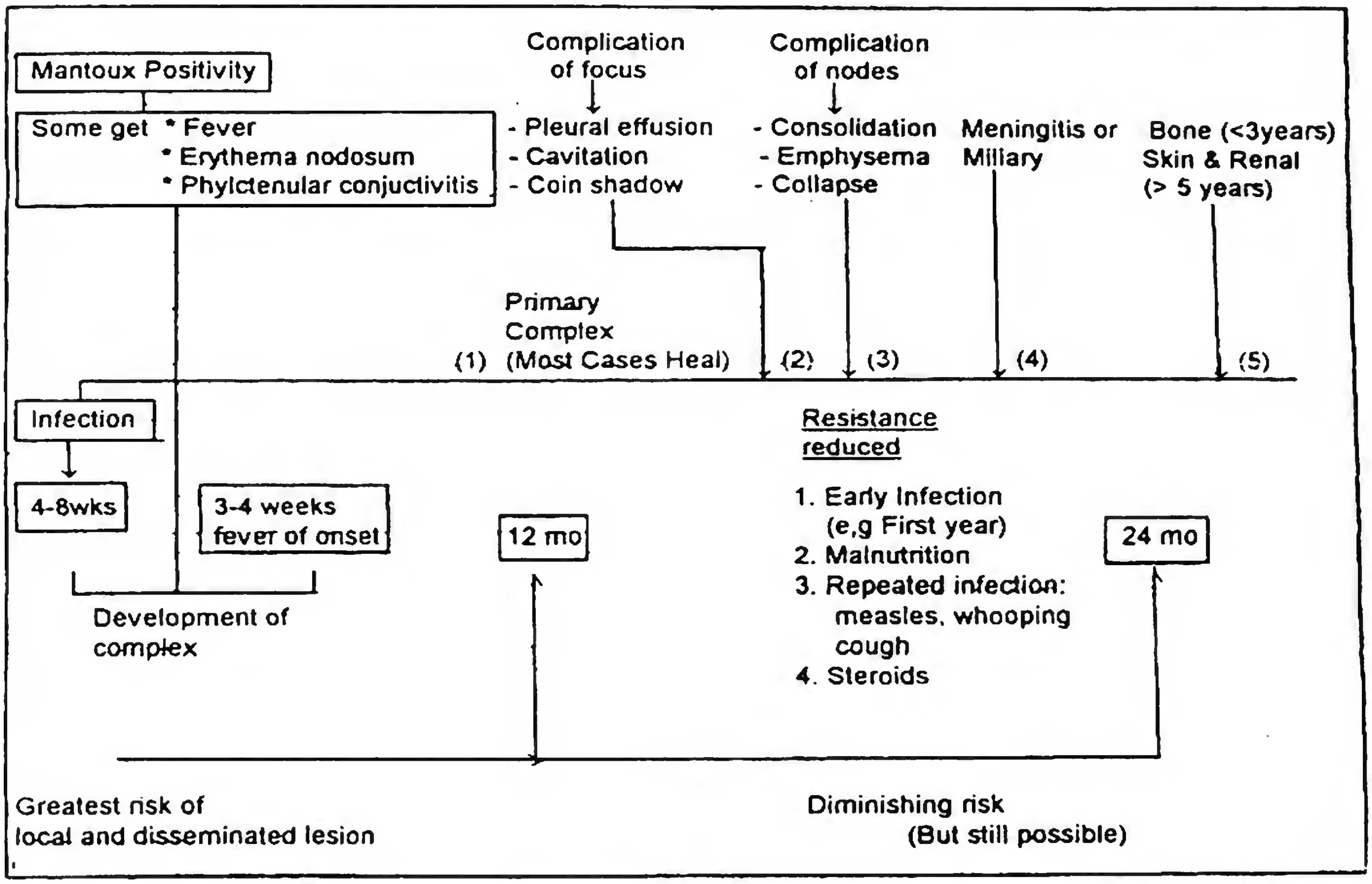
1. Failure to gain or slight loss of weight and energy over 2-3 months.
2. Sudden onset of fever with erythema nodosum, phlyctenular conjuctivitis.
3. Failure to gain weight with respiratory wheeze.
4. Sudden febrile illness with pleural pain and effusion.
5. Abdominal swelling with ascites.
6. A hard painless abdominal mass.
7. Onset of limp or painful swelling in weight bearing joint.
8. A painless firm swelling of a superficial lymphnode with smaller satellite nodes.
9. Any lymphnode abscess particularly of slow onset.
10. Subcutaneous abscesses or skin ulcers without any obvious cause.
11. A child who undergoes an unexplained change of temperament with irritability and fever, sometimes vomiting and headache.
12. Any child who fails to make a return to normal health after intercurrent infection e.g. measles, whooping cough or streptococcal tonsillitis.
13. Children with signs of space occupying intracranial tumor or of diffuse encephalitis.
14. Child with painless haematuria or pyuria.

HIV infection and Childhood Tuberculosis: HIV infection has direct and indirect effects on childhood tuberculosis. The direct impact is illustrated by the rapid progression of tuberculosis from infection to disease in children, who acquired HIV infection by vertical transmission[10]. The indirect effect is by increasing the pool of adults with active tuberculosis, thus strongly raising the probability of transmission of tuberculosis from adults to HIV infected and non-infected children living in the same environment[11]. Extrapulmonary tuberculosis occurs more often, as lymphohematogenous spread is more common in the HIV infected when compared to similar mode of spread in immunocompetent children with tuberculosis. Further, CNS tuberculosis also appears to be more common in

Table -2: Childhood Tuberculosis Vs Adult Tuberculosis[3].

	Childhood Type (Primary Infection)		Adult Type (Reinfection or Reactivation)
1.	Infection occurs for the first time and there is no allergy initially, which develops in 4-8 weeks.	1.	The tissues have already acquired allergy and immunity by prior infection and tissue response differs. Most of the adult type disease is due to reactivation of primary tuberculosis, but exogenous infection can also occur.
2.	Allergy plays a main role in development of various lesions e.g. edema, necrosis and hemorrage in lymphnodes.	2.	Tubercle bacilli play the main role and not the allergy.
3.	There is a significant enlargement of mediastinal lymphnodes.	3.	There is no significant hilar or regional lymphadenopathy.
4.	Tubercle bacilli spread is lymphatic and hematogenous.	4.	The disease is localized to one organ due to prior immunity (usually lungs). Chronic pulmonary tuberculosis is the main problem and hematogenous spread is uncommon.
5.	Major cause of morbidity and mortality is extra-pulmonary tuberculosis especially TBM, miliary or disseminated TB.	5.	The main cause of death and disability is pulmonary TB (>70%).
6.	Healing is by calcification, though segmental lesions may heal and leave residual fibrotic lesions.	6.	Healing is by fibrosis.

Fig.-1 Evolution and time table of untreated primary tubercular infection*


Mantoux Positivity
Some get • Fever
• Erythema nodosum
• Phylctenular conjuctivitis
Complication of focus
- Pleural effusion
- Cavitation
- Coin shadow
Complication of nodes
- Consolidation
- Emphysema
- Collapse
Meningitis or Miliary
Bone (<3years)
Skin & Renal (> 5 years)
(1) Primary Complex (Most Cases Heal)
(2)
(3)
(4)
(5)
Infection
4-8wks
3-4 weeks fever of onset
Development of complex
12 mo
Resistance reduced
1. Early Infection (e,g First year)
2. Malnutrition
3. Repeated infection: measles, whooping cough
4. Steroids
24 mo
Greatest risk of local and disseminated lesion
Diminishing risk (But still possible)

HIV infected children as compared to non-infected children[12]. However, there is scaricity of data available regarding the impact of HIV infection on otherwise different usual presentations of tuberculosis in children.

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"VEGETABLES, FRUITS, ANTIOXIDANTS: PROTECT THE BODY FROM RUSTING AWAY?"

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Antioxidants have been the centre of much media attention in recent years. This is because of the free redical oxidative damage has been implicated in the disease pathophysiology. Today, free radicals are known to be involved in the pathophysiology of cancer, heart disease, senile dementia, diabetes, degenerative diseases not caused by infective agents[1]. A diet rich in fruit and vegetable are key sources of antioxidants.

Free Radicals and Other Oxidants:

In 1954, Dr Harman working on free radical theory of aging, implicated free radical as the cause of degenerative changes in the human body, leading to aging[2]. A free radical has been defined as any species capable of independent existence that contains one or more unpaired electrons".[3] Discontended with such a confromation, it will try to seek stability either by donating its electron to other molecules or acquiring an extra electron from adjacent molecules. Thus such species are highly reactive. However, the remainder of the attached molecule then possesses an unpaired electron and has therefore become a free radical. This begins a chain reaction. Once the process is started, it can cascade, finally resulting in disruption of a living cell. Oxidative stress in human biology comes from a variety of sources[4]. Free radicals disrupt the equilibrium of biological systems by damaging their major constituent molecules, leading eventually to cell death. Polyunsaturated fatty acids within cell membranes and lipoproteins are particularly susceptible to oxidative attack (Lipid peroxidation, often as a result of metal Ion-dependent hydroxyl radical formation[5]. These peroxidative processes play a role in adherogenesis[6]. Following initiation by a single radical if oxygen is present, long chains of lipid peroxides may be formed by a rapid free radical chain reaction causing serious disruption of cell membrane function[7]. The generation of free radicals is an integral part of normal cell metabolism. Several path ways in aerobic cells lead to the production of free radicals such as supgroxide anion O_2 hydrogen peroxide H_2O_2, Hydroxyl radical, OH. Each new cell protects itself from damage by producing free radical scavengers such as enzymes that neutralize free radical scavengers within a cell. This balance is a key factor for preventing the development of noxious processes at the celluar and tissue level[1].

Environmental pollution and tobacco smoke form a major source of free radicals and subsequent oxidative damage in addition to those produced by normal bodily processess. The free radicals bind with vital molecules, promote mutations, clog cell membranes, impair mitochondrial function thus causing widespread damage which contributes to the development of a host of chronic diseases. Free radicals induce damage to DNA causing destruction of bases and deoxyribose sugars or single and double stranded breaks[8,9]. These events have been implicated as a cause in mutagenesis, Carcinogenesis and cell death[10].

Antioxidants:

Substances whose presence in relatively low concentations significantly inhibits the rate of oxidation of the above targets are defined as antioxidants. They are either natural antioxidants (normally presents in the body) and synthetic compounds with antiodidant activity. Antiodidants may be:

i. Enzymes like superoxide dimutase (SOD), catalase and Glutathione peroxidase.
ii. Preventive antioxidants causing sequestration of metal ions like transferrin, ceruloplasmin and albumin.
iii. Scanvenging (Chain - breaking) antiooxidants like Ascorbic acid (Vit. C), Uric acid, bilirubin, thiols, Tocopherol (vit.E), B-carotene, Ubiquinol, flavonoids and estrogens, synthetic antioxidants for pharmacological use are available. Selenium supplementation can increase glutathione peroxidase activity. "A synthetic selenium containing compound, ebselen, has been developed as glutathione peroxidase mimic[12]. Desferoxamine is a powerful synthetic iron chelator that inhibits iron-dependent lipid peroxidation and is used for iron-overload

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diseases such as thalassaemia[13] Chain-breaking antioxidants like Vit.C and Vit. E contribute to lipid antioxidant defence[14]. Some drugs have probably significant free radical scavenging effect in vivo-like probucol[15], salicylates[16] and 21-aminosteroids or "Lazaroids" which inhibit iron-dependent lipid peroxidation and can inhibit brain or spinal cord injury resulting from stroke or trauma in animals[17]

The antioxidant Hypothesis & their role:

Free radical chain reactions are being shown to be central pathophysiological features of a disease. These reactions are broken by antioxidants[1]. The experimental data support the hypothesis that peroxidative processes play a role in atherogenesis[6] The antioxidants prevent damage to low-density lipoproteins (LDL)[18] and atherosclerosis as well as peroxidative products found in blood and the arterial wall can be reduced with antioxidant supplementation[19,20]. Recent research has been focussed on role of antioxidant therapy in various diseases.

Atherosclerosis:

Majority of premature deaths are due to clinical sequelae of atherosclerosis such as strokes and myocardial infarction. Oxidation of LDL particles is a critical event in the development of the atherosclerotic plaque[6]. The oxidative-modification hypothesis of atherosclerosis resulted in trials for antioxidant defence of LDL particles. These include tocopherol (Vit.E), B-carotene and ubiquinol-10 which reduce the susceptibility of core fatty acids to oxidation[21]. Epidemiological surveys in humans link low plasma levels or dietary intake of antioxidant vitamins (Vit C, Vit. E, B-Carotene) with ischaemic heart disease[22-25]. The protective effects of Vit.E has been recently shown in the two large studies[26,27] and carotenoid intake has been shown to reduce the atherosclerotic plaques[26]. The cholesterol lowering Atherosclerotic study (CLAS)[29] which was a randomized serial coronary angiographic trial demonstrated that aggressive LDL - cholesterol reduction with colestipol niacin and cholesterol-lowering dietary therapy reduces progression of coronary atherosclerosis[30]. Consistency between Vitamin E intake and reduced coronary artery lesion progression in CLAS and angiography data consistant with the inverse correlation between plasma Vit. E levels and ischamic heart disease mortality[31] and risk of angina pectoris[23], indicate a promising role for antioxidant vitamins in primary prevention.

Hypertension:

An increase in magnesium intake has been sugested to lower blood pressure[32]. Hypertensive patients have lower levels of antioxidant vitamins particularly vitamin C[33] and infusion of antioxidants can reduce high blood pressure[34]. There are studies which show that antagonism and inactivation of nitric oxide vasodilatation is caused by superoxide radicals[35-37]. Antithypertensives like captoprill, B-blokers and calcium channel antagonists are also shown to have some antioxidant effect[38].

Diabetes Mellitus:

Increased production of free radicals has been shown to play an important role in the pathophysiology of various complication of diabetes mellitus[39,40]. In diabetics glucose combines with serum proteins and lipoproteins in a nonenzymatic glycation reaction and may auto oxidise in situ, generating free radicals and causing local oxidative damage[41]. Ascorbic acid (Vit C) metabolism is defective in diabetic patients[42]. Decreased activity of various antioxidants in serum have been reported in patients with diabetes[43] and hence is a major risk factor for development of diabetic complication. In addition to ascorbic acid, Vitamin E has also been shown to prevent glycation of proteins and therefore, complication of diabetes mellitus[44].

Carcinogenesis:

Many studies have revealed that dietary carotenes, vitamin C and Vit. E have protective effect against development of human Cancer[45,46]. Smoking is a well established risk factor in development of cancer. It causes increase in free radicals and can induce DNA damage in vitro which is preventable by antioxidant intake[47]. In eight prospective and 18 of 20 retrospective studies, lung cancer risk was reduced at high levels of vegetable and/or fruit consumption or at high intake or carotenoids or vitamin C which are markers of vegetable and fruit intake[48]. The role of B-carotene and antioxidant nutrients in prevention of oral cancer has been shown by many studies[49,50]. The epidemiological evidence cooncering vitamin C and gastric cancer has been the subject of several excellent reviews[51] Low serum levels of beta-carotene and vitamin E has been reported in gastric dysplasia[52]. Vitamin E has been shown to reduce prostate-cancer incidence and mortality by one-third in smokers according to the results of a large primary prevention trial in finnish men[53]. In a study 29,000 male smokers were randomly assigned to receive 5,0 mg alpha-tocopherol, 20mg B-carotene, both or placebo daily for upto 8 years. At the end of study the incidence was 32% lower and mortality 41% lower, in men taking alpha-tocopherol with or without B-carotene, than in those not taking the vitamin.

Ageing:

Many age related problems have been shown to be due to increased free radical accumulation Free radical destruction is thought to be a contributing factor to the decline in memory and motor performance seen in aging[54]. The common problems of increasing elderly population, senile macular degeneration and Cataract formation has been linked to free radical oxidative activity because of reduced antioxidant defence[55]. These might be prevented by appropriate nutritional advice[56,57]. Cognitive decline seen from agig may be prevented by antioxidants. Dermatological photoprotection by antioxidants can reduce the skin aging[58]. Since age-related declines in antioxidants has been demonstrated their use might help prevent many age-related diseases.

Inflammatory diseases:

In an inflammatory process there is local oxidative stress because the cells produce superoxide, hydrogen peroxide and hypochlorite primarily as an anti-bacterial killing machanism[59]. But in excess amourts they cause local tissue damage[60]. In Rheumatoid arthritis, free radical activity in inflammed joints probably contributes to their destruction. Antioxidant therpy to prevent the tissue damage are needed in these patients. Severe localized inflammation leading to ulceration and perforation of the gut wall occurs in patients with inflammatory bowel diseases (Ulcerative colitis and crohn's disease) Increased neutrophil-related oxidant activity has been associated with active disease[61]. Oxidative damage is involved in the pathogenic process of idiopathic chronic inflammatory bowel disease but the clinical efficacy of antioxidant awaits definite clinical proof, though specific intervention in the oxidative cascade has shown promising results in animal model is as reported by Kruidenier et al[62] in 1998. Oxidative injury has also been implicated in acute chronic pancreatitis[63] and the frequency and severity of attacks can be significantly reduced by antioxidant therapy[64].

Neurlogical diseases:

The brain may be particularly vulnerable to the damaging effects of free radicals because it is relatively deficient in antioxidants to begin with. Free radical oxidative stress is more associated with age-related disorders such as Alzheimers and parkinson's diseases. A possible source of radicals in idiopathic parkinson's diseases may be the oxidative metabolism of dopamine which generates peroxides. Increased iron and aluminium have also been found in Parkinsonism in brain as well as decreased glutathione, hence antioxidant therapy may be beneficial[65]. Monoamine oxidase inhibitor like selegiline slows the natural progression of disease due to decreased radical formation[66].

Hypoxic and traumatic insults lead to free radical oxidation in brain and spinal cord because of their high lipid content and poor iron-binding capacity[54]. Post-traumatic neuronal degeneration is also thought to be due to free radical induced lipid peroxidation[67]. Therefore use of antioxidants may enhance recovery. They have been shown to be effective in animal models of trauma. Tocopherols are also showing promise as neuroprotective agents[68]. The antioxidants, therefore, are useful agents to prevent age-related decline in memory & congnitive functions, and neurdegenerative disorders.

Miscelleneous:

Antioxidant therapy has been reported in many other diseases Tocoperol supplements decrease the incidence of intraventricular haemorrhage[69] and retinopathy[70] of prematurity when neonates are exposed to high oxygen concentrations. The imbalance of oxidative damage and antioxidant defence has also been described in patients with chronic renal failure[71], Preeclampsia[72], Chronic adult periodontitis[73], respiratory diseases[74], variety of haematological disorders[75] AIDS[76] and in critically ill patients[77]. The use of antixidant therapy in muscle disorders has recently been reviewed[78].

Conclusion:

Consumption of vegetables, fruits which are rich sources of various antioxidants exert a protective effect against two important cause of premature death, atherosclerosis and cancer. A human intervention study with vegetable products like tomato, carrot or spinach resulted in a significant decrease in endogenous level of strand breaks in lymphocyts DNA and oxidative base damage was also significantly reduced. Strawberries and spinach are high in antioxidants and also contain many phytochemicals or plant chemicals that appear to have antioxidant properties.

Carrots, dark green leaf vegetables and yellow & red fruits (Apricot, Melon, Pumpkin) are rich sources of carotenes. Potato, Cabbage, green pepper and citrous fruits, oranges are rich in vitamin C. Whole grain cereals, Nuts and vegetable oils are rich in Vit. E. Vegetables, fruits, beverages and tea also provide us with poly phenolic compounds known as flavonoids which are also protective antioxidants agents ischaemic heart disease[79]. So we conclude that yet plenty of vegetables, fruits, drink tea and be sure to get some kind of exercise every day. Health requires protection against free radical injury and nature has provided enough antioxidants in fruit and vegetables. There is powerful evidence that antioxidants can prevent many diseases and reduce atherosclerosis. Large prospective studies are needed before prophylactic antioxidant supplements are prescribed. This will take many years and hence eating diets rich in antioxidants seems to be the safest approach. Schlipalius[10] writes "Further medical trials will add to our knowledge of how the carotenoids and the other micronutrients work in our bodies and their benefits of health. Unfortunately, our human bodies are so comples that it takes a long time, with repeat trials being necessary for us to have confidence in the results. This is frustrating for those of us, myself included, who would like to know now, not later, how we can optimise our ever-reducing years of enjoyable life.. All we can do is to watch the research trends as they appear. I trust that you and I will be so well norished in micronutrients that we live long and healthy and see the outcome of research far into the future".

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NEWER IMMUNOSUPPRESSIVE MEDICATIONS FOR KIDNEY TRANSPLANTATION

Tajammul Fazili M.S., D.N.B.

When the history of organ transplantation is written, the 1990's will very likely be referred to as the decade of new immunosuppressive agents. The excellent results of kidney and other solid organ transplants that led to widespread acceptance of transplant procedures in the 1908's were achieved with relatively limited therapeutic armamentarium. This consisted mainly of corticosteriods, azathioprine and cyclosprine. The addition of monoclonal and polyclonal antibodies was a big leap forward. The 1990's have witnessed the discovery of a new generation of immunosuppresants, some of which have not yet crossed the clinical threshold. The great success of organ transplantation that has been achieved in the 1990's with currently available agents is paradoxically, making it exceedingly difficult (and enormously expensive) to prove the added benefit of new agents.

Monoclonal and Polyclonal Antibodies

Various polyclonal-antibodies-antilymphocyte globulin (ALG) and antithymocyte globulin (ATG) have been available for use in clinical transplantation for more than two decades. Currently the only polyclonal antibody widely available is anti-thymocyte globulin (ATG). The monoclonal antibody muromonabl CD3 (othoclone OKT3-"OKT3") has been available for clinical use since the late 1980's.

OKT3

Monoclonal antibodies are produced by the hybridization of murine antibody-secreting B lymphocytes with a non-secreting myeloma cell line whose neoplastic potential permits the secretion of antibody in perperity. OKT3, directed against the CD3 antigen complex found on all mature human T cells, is currently the only commercially available monoclonal antibody for therapeutic use. It is a highly effective, yet potentially toxic drug. Its introduction into clinical transplantation was the most important therapeutic advance since the advent of cyclosporine. It is most frequently used for the treatment of episodes of steroid resistant rejection that may also be used with great effect as primary rejection treatment, for rejection prophylaxis, or for induction therapy in the immediate post-transplant period. The standard dose of OKT3 is 5mg given as an IV bolus through a milipore filter. The standard course consists of a daily dose for 10 days. Side effects include fever with rigors and chills, pulmonary edema, nephrotoxicity and post-transplant lymphoproliferative disorders.

Polyclonal Antibodies

Polyclonal antibodies are produced by immunizing either horses or rabbits with human lymphoid tissue and then harvesting the resultant immune sera to obtain gama globulin fraction. The only widely available polyclonal antibody is ATG. Polyclonal antibodies are effective agents for rejection prophylaxis in the early post-transplant period and for treatment of steroid resistant rejection. Polyclonal antibodies are given in a dose of 10-20 mg/kg/day for 7-14 days. The antibodies are mixed in 500ml of normal saline and infused over 56 hours in a central vein. Side effects include fever and chills, arthalgias, occasionally anaphylaxis or a serum sickness like illness, rarely thrombocytopenia and leukopnia have been reported.

Tacrolimus

Tacrolimus (Prograf) formerly known as FK 506, is a macrolide antiboitic compound isolated from streptomyces. It is ten times more potent than cyclosporine on a weight basis. Although tacrolimus is structurally unrelated to cyclosporine, its mode of action is very similar. Like cyclosporine it binds to a specific intracytoplasmic binding protein (FKBP) and the combination of the drug and its binding protein block and action of calcineruin probably by impairing access to its phosphatase site. Tacrolimus and cyclosporine must not be administered simultaneously because of the potential for synergistic toxicities.

Tacrolimus is available in an I.V and an oral formulation. The recommended starting dose is 0.15-

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0.30 mg/kg/day administered in a split dose each 12 hours. It is metabolized primarily by the liver P 450 III A system and excreted through the biliary system.

The toxicity profile of tacrolimus is similar to that of cyclosporine and includes nephrotoxicity, a hemolytic uremic syndrome, hyperkalemia and hypomagnesemia. Headaches, insomnia, parasthesias, pruritis and a course tremor have been reported. Nausea, vomiting and diarrhoea are common in patients receiving tacrolimus.

Mycophenolate Mofetil

Mycophenolate mofetil (Cellcept) (MMF), previously known as RS61443, is a promising new immunosuppressive drug. The active compound is my cophenolic acid (MPA), a fermentation product of several penicillium species, the mofetil moiety serves to markedly improve its oral bio-availability.

MPA is a reversible inhibitor of the enzyme inosine monophosphate dehydrogenase (IMPDH). IMPDH is a critical rate limiting enzyme in the synthesis of purines and catalyzes the formation of guanosine mucleotides from inosine.

MMF is generally well tolerated and after oral administration is rapidly absorbed and converted to MPA. The most common adverse events are related to the GI tract, with diarrhoe occurring is approximately one-third of the patients, esophagitis and gastritis in approximately 5% and GI hemorrhage in 4%. Leukopenia and anemia have also been reported. Azathioprine and MMF should not be administered concomitantly. Nephrotoxicity, neurotoxicity and hepatotoxicity have not been reported.

Sirolimus

Sirolimus (Rapammune), formerly known as rapamycin, is a macrolide antibiotic, structurally related to tacrolimus. Combined use of the two drugs is contraindicated. Sirolimus may have a synergistic effect with cyclosporine.

Other Experimental Immunosuppresants

Deoxyspergualin

15-Deoxyspergualin trihydrochloride (DSG) is an anti-tumour antibiotic that has been found to facilitate organ acceptance in animal models. The drug is typically administered as a slow I/V infusioin in a dose of 3-5 mg/kg/day over a 7-10 day period.

Mizoribine

Mizoribine, also of antibiotic origin, exerts its immuno-suppressive effects as a metabolic antagonist of purine synthesis. It has been used synergistically with cyclosporine and prednisone with minimal side effects.

Cyclosporine OG-37-325

Cyclosporine OG-37-325 has a structure that is similar to the familiar cyclosporine A. Its action is also very similar. The clinical development of the compound has been discontinued.

Brequinar Sodium

Brequinar sodium is an immune-suppressive agent with a mode of action very similar to MMF. It impairs pyrimidine metabolism. Clinically significant thrombocytopenia has been associated with its use.

Leflunomide

Leflunomide is a promising new immunosuppressive agent. It is structurally unrelated to any of the compounds currently in use or under investigation. Its action may be synergistic with cyclosporine.

New Monoclonal Antibodies

Despite pioneering work, OKT3 remains the only monoclonal antibody in routine transplantation practice.

Newer monoclonal antiboidies under development include CD 45 molecules, BIRRI, anti-Tac antibodies, and T10B9. Anti-CD4 monoclonal antibodies may block the interaction between the T cell receptor and the polymorphic determinants of class II antigens. Humanized monoclonal antibodies exploit genetic engineering techniques combine a rodent-derived most successful product of the attempt to humanized several of the rodent antibodies is the monoclonal humanized anti-tac (zenapax) (HAT) antibody. It has been reported to be safe for human use.

Donor-Specific Bone Marrow and Blood Transfusion

Infusion of donor-specific bone marrow in combination with short term non-specific immunosuppression using polyclonal antibodies has produced long term graft survival in the absence of immunosuppressive therapy in experimental and clinical organ allografts. The tolerogenic effect of bone marrow and blood may be due to the development of a state of microchimerism.

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SEROLOGICAL STUDY OF BRUCELLOSIS IN KASHMIR - 5 YEARS APPRAISAL

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Abstract: Serum samples of six hundred and thirty two suspected cases of Brucellosis in the mean age group of 30 years were analyzed for Brucella agglutination titre. One hundred and thirty seven -137(21.7%) samples were found having significant titres of 1:80 or more. Percentage positivity distribution for Brucella abortus and Brucella melete isis detected was 12.7% and 9% respectively.

Titre-wise distribution for 1:80; 1:160; 1:320; 1:640 and 1:1280 was 45(32.8%), 58(42.3%); 10(1.5%), 24(2.7%) and zero in that order respectively. Most of patients lived in low lands and majority were butchers and shepherds. A history of animal contact and ingestion of raw milk were important factors in disease transmission. A higher prevalence was found in males with mean age 30 years. No seasonal variation was encountered. The findings depict a rapid increase in brucella cases in Kashmir valley thereby making it mandatory to include brucella agglutination test as a frontrunner in the panel of tests for investigating PUO cases in this part of country.

Key words: Brucella, Agglutinins, Significant titre

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Introduction

Brucellosis, a world wide problem, is a zoonotic disease primarily affecting goats, sheep, cattle, pigs, buffaloes and is transmitted to man by contact with infected animals and through their products[1]. Brucellosis is known under various names such as mediterranian fever, malta fever or undulant fever. Bruce in 1887[2] described Brucella abortus as being carried by cattle. Subsequently Zamit in 1905 demonstrated that brucella meletensis was carried by goats and excreted in their milk.

Humans get infected by close animal contact or consumption of infected animal products by bacteria of genus Brucella[3,4]. Other means of infection include skin abrasions or inhalation of airborne particles[5,6].

The clinical diagnosis of brucella is difficult because of protean nature of the disease, varying from acute febrile illness to low grade chronic disease (Farreli et al 1975)[7]. Laboratory diagnosis depends mainly on detection of specific antibodies from blood. Isolation of brucella organism from blood and tissues is very low to the tune of 10-12 percent (Wilson and Miles 1964)[8]. Four types of tests used to detect brucella antibodies are agglutination, complement fixation, indirect haemagglutination and modified indirect Coomb's test (Panigreh et al 1979, Kerr et al 1968)[10]. Brucella agglutination test remains the most commonly used one as it is cheap and less cumbersome.

Presence of antibody against the organism has certain limitations which is to be noted while interpreting the results. One of them being the presence of antibodies in normal population and the other being the variations in the level of antibodies against brucella in various parts of India. We report here the result of our study to evaluate the level of brucella antibodies in cases of fever of unknown origin. An attempt has also been made to find out age, sex, occupation and seasonal distribution of cases.

Material and Methods

Serum Samples five ml venous blood from 632 suspected cases of brucellosis at Sher-i-Kashmir Institute of Medical Sciences, Srinagar was collected from time to time over a period of 5 years from September 1994 to August 1999. Serum samples were preserved in 1:1000 dilution of thiomersal and kept at -20°C in small aliquots till used. Before use, each sample was inactivated at 56°C for 30 minutes.

History of occupation, age, sex, drinking of raw milk, animal contact, exposure to manure and month of illness were recorded for each study case. One hundred control samples consisting of healthy hospital personnel were also included in the study.

Brucella agglutination test:

The test was carried out as described by Kerr et al

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(1968)[10] with some modifications from directions on kit catalogue. Test was performed in round bottomed agglutination tubes 7.5cmx1cm with serum dilutions starting from 1:20 to 1:1280. 3+(50 percent) or more agglutination was considered as positive. Titres were expressed as international units. Each test sample batch was put alongwith positive and negative control to reduce the margin of technical error. A titre of 1:80 or more was taken as significant as was described earlier also[10,11]. Standard tube agglutination was used for both Br. abortus and Br. meletensis in serial dilutions of patients' serum[12]. Brucella antigen suspensions were obtained from Wellcome Research Laboratories (Dart Ford, United Kingdom). Blood cultures were not put simultaneously as most of the patients gave history of antibiotic intake before submitting blood sample for testing in our laboratory.

Results and Discussion:

Out of six hunndred and thirty two sera tested from cases of PUO, one hundred and thrity seven patients (21.4%) showed Brucella agglutination at significant level ranging from 1:80 to 1:640. Out of 137 positive cases, 58(9.1%) had titres of 1:640 and 24(3.7%) showed titre of 1:320. Ten sera (1.5%) and 45 sera (7.1%) depicted titres of 1:160 and 1:80 respectively. Four hundred and ninety-five sera (78.6%) showed presence of Brucella agglutinins in low non-significant titres (Table-I).

Table-1: Results of agglutination test against Brucellosis

Type of cases	No. of Sera tested	end titres obtained.						
		1:20	1:40	1:80	1:160	1:320	1:640	1:1280
Pyrexia of unknown	632	145 (22.9)	350 (55.3)	45 (7.1)	10 (1.5)	24 (3.7)	58 (9.1)	0
Controls (Hospital personnel)	100	56	42	2	0	0	0	0

Figures in parenthesis show percentage.

Positive agglutination titres were obtained with 137(21.4%) sera obtained from PUO cases as compared to 2% cases of hospital personnel who served as controls. Species wise distribution percentage revealed 12.7% and 9% positivity for Brucella abortus and Brucella meletensis respectively.

The highest concentration of agglutinins against Brucella found in control sera from hospital personal was 1:80. This level of antibody titre was however found only in 2% cases.

In the Indian literature base levels of Brucella agglutination have been worked out (Mathur, 1955[13]; Sivarajan et al 1965[14]; Chitkara et al 1966[15]; Sen et al 1970[16]; Mahakur et al 1972[17]; Farreli et al 1975[7] and Panigreh et al 1979[9]) as same is always desirable amongst people with occupation at great risk of acquiring brucellosis.

Single base level agglutination titre is good enough for the tests as far as normal population is concerned[9]. Seroagglutination tests play an important role in the laboratory diagnosis of pyrexia due to Brucella. Cultivation and identification of bacteria are not always possible due to inadequate laboratory facilities and prior treatment of cases by antibiotics and chemotherapeutic agent. The prevalence of Brucella agglutination among 632 cases of PUO in the present study is 21.4 percent thereby showing more than ten-fold rise as compared to an earlier study of 1968 (Anand, 1968)[18]. It is also quite high considering that percentage positivity varies from 0.09 percent in Aligarh to 5.08 percent in Delhi as per earlier reports of such studies in Indian subcontinent (Table-2).

Table-2: Prevalence of Brucellosis in India

Author/year	Place	Total cases	Percentage positive for Brucillosis
Singh (1964)	Delhi	210	0.91
Chitkara & Kaur (1966)	Punjab	1648	2.8
Anand (1968)	Kashmir	500	1.4
Mathur (1969)	Haryana	5296	3.34
Joshi and O.Prakash (1971)	Delhi	600	5.98
Bal & Tyagi (1971)	Aligarh	1050	0.09
Koshi et al (1971)	Vellore	174	0.50
Mahakaur & Panda (1972)	Burla	215	3.72
Sharma et al (1974)	Aurangabad	1016	1.08
B.K. Nanda et al (1979)	Berhampur	600	2.9

A high sex prevalence was found in males with highest age prevalence between 28 and 32 years. Out of one hundred and thirty-seven positive cases, one hundred and three were males and thirty four females. The ratio between male and female was 3:1.

Seventy-two percent of cases showing positive result belonged to age group 28 to 32 years and none below 10 years. Rhandwa in 1974[19] reported a high incidence of brucellosis during summer. In our study, we could not appreciate any seasonal predominance. The cases were almost equally distributed throughout the year. Ecology of Kashmir consists of highlands which is extension of Himalayan mountains. These mountains surround the lowlands of Kashmir Valley. Good percentage of population in Kashmir consists of shepherds and butchers who depend mainly on animals. Also few people consume raw meat and unboiled milk.

Summary

The agglutination test for brucellosis was performed in 632 cases of PUO and in 100 control sera significant titres of 1:80 and above were detected in 21.7% of suspecterd brucellosis cases which is quite high by all means. The ecology of Kashmir and occupation of some Kashmiris contribute to the high prevalence of brucellosis here. In the context of present study, Brucella agglutination test should be mandatory for investigating all PUO cases. Also anti-microbials should be avoided unless patients of PUO give blood samples for testing.

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AN OUTBREAK OF NOSOCOMIAL KLEBSIELLA PNEUMONIAE SEPTICEMIA AMONG NEONATES IN SKIMS

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Abstract: Eleven consecutive cases of Klebsiella septicemia occuring in the level III care Neonatology department were studied over a 12 day period. The babies were preterm and had other perinatal risk factors. Microbiological tests of the neonates, the environment and the staff confirmed the contamination of heparin saline with Klebsiella pneumoniae being used to flush intravenous cannulas. Phenotypic studies (antibiogram and capsular typing) revealed that the same strain was present in heparin saline, as was isolated from among the septicemic neonates. Thus the source of infection was identified and eliminated, mortality was found to be 45.4%.

Key words: Klebsiella pneumoniae, Neonatal septicemia, Nosocomial infection.

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Introduction:

Neonatal septicemia is an important cause of perinatal mortality in the developing world. Klebsiella is emerging as an important cause of nosocomial infection in NICU, and the serotypes isolated are often resistant to multiple antibiotics[1,2].

Intrinsic patient factors that increase the risk of nosocomial blood stream infection in neonates are low birth weight, lowered immunity in preterm babies and severe underlying illness. Treatment factors such as indwelling devices, intensive care unit stay, longer hospital stay, also increase the risk of blood stream infection.

Inadequate space, shortage of staff, a high occupancy rate, wide spread use of antibiotics and increased susceptibility of the population, all predispose to early colonisation and subsequent infection by virulent Klebsiella strains, resulting in high morbidity and mortality[3].

Contamination of infusates has been documented as a cause of device associated sepsis[4,5,6]. Thus contamination may enter the system through heparinised flush solution. Catheters irritate vascular intima and provoke thrombogenesis which is associated with increase risk of infection.

We report an outbreak of Klebsiella pneumoniae among neonates due to use of contaminated heparin saline which had been prepared in advance and was used to flush intravenous cannula. This was probably contaminated either during the preparatory stage or due to unhygienic handling of heparin saline.

Material and Method:

This study is based on 11 neonates admitted in the level II and Level III ICU of Neonatology department of Sher-i-Kashmir Institute of Medical Sciences from 8th June 1997 to 15th June 1997 who developed nosocomial Klebseilla septicemia.

1. Detailed history of these neonates was recorded (obstetric risk factors, history of labour, birth weight, gestational age, date of onset, presenting clinical features, complications and duration of hospital stay).
2. The investigation done were routine hemogram, blood culture, CSF examination and chest X-ray, culture of pus, urine, stool and umbilical swab was done where needed.
3. In 11 neonates who developed signs and symptoms of septicemia a second blood culture was taken and processed as per standard methods.
4. The cultures revealing growth were subjected to biochemical tests and antibiotic sensitivity testing.
5. The Klebsiella pneumoniae isolates identified were further subjected to capsular serotyping by Klebsiella capsule typing immune sera "Seiken".

11 babies revealed on blood culture and sensitivity to be suffering from Klebsiella pneumoniae septicemia with a similar antibiogram and capsular type over a short period of time./ An immediate investigation was carried out to find the source of infection which could be eliminated.

The samples taken included; (1) nose and hand swabs from the staff of the neonatology ward; (2) Swabs from

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Table-1: Bacteriological Isolates from neonates, staff and fomites

	Name of specimen	Growth on culture	Antibiogram	Capsular serotype
1.	Heparin Saline	Klebsiella pneumoniae	S-Amikacin, Cefperazone Gentamycin Cetataxime R- Ampicillin Cefalaxin Ampiclox	CI
2.	Blood cultures 11 - No.	Klebsiella pneumoniae	Same	CI
3.	Staff member 'x'	Klebsiella pneumoniae	Same	CI
4.	I/V cannula	Coagulase negative staphylococi		
5.	Incubator	Coagulase negative staphylococci		
6.	Ventilator tubing	Pseudomonas sps		
7.	H_2O for humidifer	No growth		
8.	Floor	Pseudomonas + Aerobic spore bearers		
9.	Wall	Aerobic spore bearers coagulase negative staph.		

***Note:** Nose swab and hand swab from other members of neonatology ward on culture grew normal nasalflora and normal skin flora respectively.* R ----- Sensitive. R ----- Resistant

Table -2: Clinical profile of neonates with Klebsiella septicemia

S.No.		Age after birth	Birth Weight age	Gestation age	Date of Ist-ve blood culture	Date of 2nd +ive blood culture	Outcome
1.	Baby Falaq	2 wks	2 kgs	32 wks	9.6.97	16.6.97	Survived
2.	Baby Zarena	3 wks	18kgs	30 wks	12.6.97	19.6.97	Death
3.	Baby Sara	1 wk	2.1 kg	32 wks	12.6.97	19.6.97	Survived
4.	Baby Asmat	2 wk	2 kgs	32 wks	13.6.97	20.6.97	Survived
5.	Baby Tasa	1½wk	1.9 kg	30wks	13.6.97	20.6.97	Death
6.	Baby Masooda	1.5 wk	2 kg	30 wks	13.6.97	20.6.97	Death
7.	Baby Laila	1.2 wk	2.2 kg	32wks	13.6.97	21.6.97	Survived
8.	Baby Saami	1.4 wk	2.4kg	32 wks	14.6.97	21.6.97	Survived
9.	Baby Tahira	2.1 wk	2.3 kg	32wks	14.6.97	21.6.97	Survived
10.	Baby Sana	2 wks	1.8 kg	30wks	15.6.97	22.6.97	Death
11.	Baby Janan	2.2 wks	1.9 kg	30 wks	15.6.97	22.6.97	Death

the incubators, ventilator tubing, water for humidifier, intravenous cannula and heparin saline being used for flusing intravenous cannula. The swabs were subjected to microbiological tests as per standard method.

Heparin saline and hand swabs from staff member 'x' grew Klebsiella pneumoniae which was subjected to capsular serotyping and antibiogram.

Results:

On second blood culture, 11 of the septicemic neonates grew Klebsiella pneumoniae (Table 2) The source of infection was considered to be nosocomial in origin as the initial blood culture on admission was negative in all cases (table I). Besides these babies on admission were not on antibiotics and clinical examination did not reveal any signs of septicemia.

All of the 11 babies had underlying predisposing factors like low birth weight and prematurity which had adverse effect on the outcome of the babies (Table 1).

5 of the eleven babies who died had birth weight <2 kgs and gestational age of 30 wks or less. The othr six babies survived after prolonged antibiotic therapy.

Klebsiella pneumoniae which was isolated from all the 11 blood cultures had similar capsular serotype CI and same antibiogram as shown in Table 2.

Culture of heparin saline and one of the hand swabs from the staff member 'x' also revealed growth of Kelbsiella penumoniae with similar antibiogram and capsular serotype CI (table 2).

The phenotypic methods like antibiogram and capsular typing used to find the similarity of the strain have been assessed with capsular typing having fair discriminating power (table 3).

Table-3: Comparison of the phenotyping methods in klebsiella pneumoniae to identify the causative strain.

	Parameter	*Antibiogram*	*Capsular typing*
1.	Proportion of strains typeable	All	Most
2.	Reproducibility	Fair	Good
3.	Discriminating power	Poor	Fair
4.	Ease of interpretation	Excellent	Good

Discussion:

Nosocomial Klebsiella pneumonia epidemics have been reported to occur in the neonatal care units, secondary to contaimination of intravenous fluids[8], and due to colonization with resistant strains[9], but in most of the reported out breaks the source could not be identified[10,11,12]. In the present outbreak the contaminated heparin saline which was used to flush the intravenous cannula of all the babies who later became septicemic, led to the conclusion that contaminated during the preparatory phase or during its handling. Incidentally a staff member also grew Klebsiella pneumoniae, from the hand swab taken, with similar antibiogram and capsular type. The probable mode by which the heparin saline got contaminated was through the staff member, who probably did not follow the aseptic techniques during the handling of heparin saline. Genotypic methods though more accurate could not be done because of lack of material. Klebseilla pneumoniae was introduced into heparin saline which got subsequently transmitted to the babies. The outcome of the babies who develped Klebsiella septicemia was affected adversely by low birth weight and prematurity[13,14]. Phenotypic methods like antibiogram and capsular serotyping were used to find the similarity of the strains and source of infection. Klebsiella pneumoniae capsular type C, was found to be the causative organism, being found in all of the // positive blood cultures heparin saline and staff member 'x' indicating a common source of infection, heparin saline. All Klebsiella pneumoniae isolates shared a similar antibiogram being sensitive to ciprofloxacin, amikacin, gentamycin and cefotaxime and cefperazone and resistant to ampicillin, cephelexin, ampiclox. Fortunately the resistance in Klebsiella reported to be high against amikacin[15], has not been found in our present study.

In conclusion we would like to emphasize that infection control procedures like staff surveillance, staff education, isolation of infected babies, emphasis on hand washing and aseptic techniques could drastically reduce all nosocomial infections.

Hygienic hand washing with either 2% chlorhexidine, 2% povidine iodine, 70% isopropyl alcohol, or triclosan between the neonates should be strictly adhered to. Aseptic techniques during all invasive procudure should be followed.

Besides freshly prepared heparin should be used, along with its proper storage to prevent its contamination. Surveillance of staff members should done to isolate any carriers. The level of disinfection in the intensive care unit as neonatology should be monitored by the infection control team. To prevent infant mortality in developing countries we require a high quality neonatal care in hospitals, apart from identifying prepregnancy risks and good prenatal care.

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MINICHOLECYSTECTOMY VS CONVENTIONAL CHOLECYSTECTOMY: A PROSPECTIVE STUDY. IMPLICATIONS IN THE LAPAROSCOPIC ERA.

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Abstract: *A clinical prospective, randomized trial was designed to compare results of elective "open" conventional cholecystectomy (CC) to those of minicholecystectomy (MC). The CC group comprised 120 patients while the MC group comprised 105 patients. In the CC group, a conventional open cholecystectomy was performed through a subcostal incision, in the MC group operation through an initial 5cm subcostal incision was performed. Mean length of wound was 14cm and 5.1cm in the two groups respectively (P<0.001). Mean operative time was 60 and 50 minutes respectively. Mean operative dificulty, estimated on a 1-10 scale was 3.7 ad 5.8 respectively (P<0.05). Mean post-operative analgesia requirements (number of doses of 75 mg diclofenac sodium) were 2.5 and 1.5 respectively (P=0.002). Mean duration of hospitalization were 4.7 and 3.5 days respectively (P<0.001). Mean "overall patient satisfaction", estimated on 1-10 scale, was 6 and 8.5 respectively (P=0.002). We conclude that minicholecystectomy offers less pain, earlier recovery, and better cosmetic results than the conventional "open" procedure. Published results of MC compare favourably with those of laparoscopic procedures.*

Key words: *Cholecystectomy; Gall stone; Minicholecystectomy.*

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Introduction

Dubois in 1982[1] was probably the first to describe cholecystectomy (CC) through a minilaparotomy. Minicholecystectomy was described by Goco and Chambers in 1983[2]. Minicholecystectomy refers to an operation performed through a short right subcostal incision (4-10 cms) offering the currently much-spoken-about advantages of minimally invasive surgery[3]. The benefits of this procedure are well documented in a substantial number of papers and abstracts published since[4-11] (Table-1). The value of minicholecystectomy remains still active in this laparoscopic era, being cost effective, especially in developing countries. We perform both procedures at our centre.

Table-1: Minicholecystectomy: review of literature

Authors	Ref	Cases	Incision (cm)	Duration (min)	Hospital stay (days)
Goco and Chambers	(2)	56	4 mean	47	1.5
O'Dwyer et al	(4)	55	5 mean	61	3.9
O'Kelly et al	(5)	32	5 mean	46	3.0
Largiade'r and Rothlin	(6)	10	6-7 mean	?	?
Merrill	(7)	82	5.5 mean	65	2.0
Ledet	(8)	200	5-10 range	?	<1.0
Gubern et al	(9)	50	7.7 mean	70	4.0
Stage et al	(10)	24	6 mean	?	2.0
Morton et al	(11)	96	4-5 range	45	2.5

Patients and Methods

Two hundred and twenty five patients scheduled for elective cholecystecomy for symptomatic cholelithiasis during a period of 28 months were studied. The patients were randomized into two groups. Minicholoecystectomy (MC-105 cases, and the conventional cholecystectomy (CC) group-120 cases. The two groups were well matched with regard to age, sex, weight/height index, incidence of associated medical disease and previous abdominal surgery (Table-2).

Table-2: Patient's Characteristics

	Conventional cholecystectomy	Minicholecystectomy
No. of patients	120	105
Sex (male/female)	16/104	11/94
Median age (years)[a]	35.90±10.11	37.61±9.18
Associated medical diseases[b]	18	29
Previous upper abdominal surgery[b]	14	9

a = Values are mean±standard deviation
b = No. of patients

Operation

All procedures were performed under general anaesthesia through right subcostal incisions and single dose antibiotic prophylaxis used.

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Conventional Cholecystectomy

The length of the incision was determined by the surgeon to offer comfortable exposure. The technique of cholecystectomy was left to the discretion of the individual surgeon.

Minicholecystectomy

The patients were placed in the supine position and retractors with light source were used. An initial 5cm incision was placed over the presumed location of the gallbladder. If exposure was not adequate the incision was extended in stages each 1cm long. Both fundus first as well as duct first methods were employed according to the need and ease of dissection. The metal clips were used in some for artery and duct occlusion. The incision was closed in two layers and skin with slik sutures. Suction or corrugated drains were placed in some according to the need. The final length of incisions was measured following closure.

End Points

The difficulty of the procedure was estimated on a 1-10 scale by the surgeon and the operative time was recorded. Post-operatively, the daily degree of pain was measured by the patient on a 1-10 scale. The total amount of analgesia required and the hospital stay were registered. Three weeks after the operation patients were seen in the follow up and their " overall satisfaction" with the procedure was recorded on a 1-10 scale.

Statistical Analysis

The results were compared using the unpaired student's 't' Significant differences were assumed to exist when P<0.05.

Results

The results are summarized in Table-3. Data are presented as mean±standard deviation.

Table-3: Results[a]

	Conventional Mini- cholecystectomy	cholecystectomy	P Value
Length or wound (cm)	15±1.1	5.1±0.4	P<0.001
Operative time (min)	60±8.5	50±9	P<0.001
Operative difficulty (1-10)	3.7±0.5	5.8±0.6	P<0.005
Post-operative analgesia[b]	2.5±0.5	1.5±0.6	P=0.002
Hospital stay (days)	4.7±0.7	3.5±0.3	P<0.001
Patient satisfaction (1-10)	6.0±2.3	8.5±1.3	P=0.002

a = Values are mean±standard deviation.

b = No. of doses of 75mg diclofenac sodium.

Length of Incision

The mean length was 5.1 cm (range 4-10) in the MC group. On three occasions it was extended to 7-10 cms due to insufficient exposure in 2 obese patients and to difficult dissection of an "intra hepatic" gallbladder in one patient. The mean length in the CC group was 15cm (range 12-18).

Duration of Operation

There was difference in time taken for the procedure between the two groups. Mean duration was 50±9 minutes in the MC group and 60±8.5 minutes in the CC group (P<0.001).

Surgical "Difficulty"

Using a 1-10 scale, the MC was estimated to be significantly more difficult than the CC; mean 5.8±0.6 and 3.7±0.5, respectively (P<0.05).

Post-operative Analgesia Requirements

Patients in the MC demanded significantly less doses of 75mg diclofenace sodium than those undergoing CC; mean 1.5±0.6 and 2.5±0.5 respectively (P=0.002).

Hospital Stay

Hospital stay was significantly shorter in the MC group (mean 3.5±0.3 days) tha in the CC group (4.7±0.7 days (P<0.001).

"Overall Satisfaction"

Satisfaction was judged significantly better by patients who underwent MC, on a scale of 1-10 a mean of 8.5±1.3 was recorded as compared to 6.0±2.3 in the CC group (P=0.002).

Disability

Three weeks following operation, around 70% in the MC group and 40% in the CC group reported a full return to their pre-operative activities.

Complications

Wound infection occurred in 9 patients of MC group and 4 patietns of CC group. Respiratory tract infection occurred in 7 patients of MC group and 3 patients of CC group.

Discussion

Thirty patients were randomized in a study[11] concluding that elective cholecystectomy can equally be performed through a 6cm incision, and that hospital stay is reduced with a trend toward improved lung function and earlier return to work in the MC group. Our study shows that the morbidity of cholecystectomy is proportional to the size of abdominal incision and thus to the amount of surgical trauma inflicted to the abdominal wall; patients who underwent MC required significantly less analgesia, had shorter hospital stay, and expressed better "overall satisfaction".

The results of these trials and the others (Table 1) clearly demonstrates that MC is safe and feasible in most patients. Some have advocated it on an ambulatory basis[8] and others under local anaesthesia.[6] Common bile duct exploration if needed can also be carried out through the minilaparotomy.[3,8,9,11,12] The restricted access obviously makes MC a more difficult procedure. Inadequate exposure promoted extension of the incision in few patients in our series while others report this incidence between 6 to 20%.[2,4,5,9,11] Various methods have been employed in overcoming the technical difficulty of MC including pre-operative ultrasound localization of the gallbladder[4] and the use of head lights or lighted retractors[2] like used in our series. Some suggest use of abdominal wall muscle retraction instead of division for reducing the discomfort of the procedure[7,13].

This study would have been of greater interest to all had it compared MC to the laparoscopic technique (LC). Reddick and Olsen[14] compared results of LC with those of MC performed during the same time period and concluded that the first is followed by shorter hospitalization and earlier return to work. Barkun et al[15] prospectively randomized 70 patients to undergo MC or LC. The latter was associated with shorter hospital stayand duration of convalescence and earlier return to normal activities. Unfortunately, the length of the incisions in the MC group was not reported and a few procedures were performed through a midline incision, making the definition of MC in this study doubtful.

The large accumulated published data leads us to believe that MC compares favourably with LC.[2-12,16] The total wound length is slightly longer in MC than in "four ports" LC[5] and post-operative analgesia requirements appear too be identical or only slightly increased in the MC groups. Short hospital stay and faster convalescence are the main advantages attributed to LC. However, the duration of hospitalization after MC ranges between a few hours,[8] 1.5 days,[2] and 3 to 4 days in this series and others.[4,9] Hence, timing of discharge depends on multiple doctor and patient related factors and cannot, thus, be compared properly in multicenter randomized trials. Interestingly, even CC can be performed as an outpatient procedure[17].

In terms of patiennts comfort and recovery, LC appears equal to MC or perhaps slightly better. With regard to the icidence of complicatios, elective "open" convenntional cholecystectomy has proven to be an extremely safe operation, associated with almost no mortality and minimal rate of surgical complications, and hence it is the gold standard to which all "new" procedures should be compared.[18,19] Evidence represents that LC has inherently more dangerous approach, producing a substantial rate of avoidable deaths and biliary complications.[20] Conversely, MC affected by the traditionally secure "open-retrograde"manner has proven a very safe operation, the results of 2000 cases have revealed no mortality or common bile duct injuries.[21] Additional potential disadvantages of LC include: higher equipment costs, longer operating room-time (and innstrument service), high conversion rate, need for new skills, and emergence of a new generation of young surgeons with inadequate exposure to open biliary surgery.

Baxter ad O'Dwyer[21] believe that the laparoscopic and minilaparotomy techniques would be found so similar that they could be used interchangeably. We wish to add that a larger member of patients should be studied to prove that the laparoscopic approach is as safe. MC and LC can be cosidered easier on the patiet than the CC. In selected cases LC might save a day or 2 of hospital care and analgesics, but in emergencies in busy surgical setting, in patiets with previous abdomial operatios, MC is a good alternative. Also for conversion of LC to open procedure, MC seems to have a place. MC also appears to be cost effective especially in developing and uderdeveloped countries.

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A RETROSPECTIVE ANALYSIS OF CASES OF ADVANCED URINARY BLADDER CARCINOMA TREATED WITH SURGERY AND RADIATION THERAPY

Satish Sharma M.S.; R. Kapoor M.D.; Kuldeep Sigh M.D.; R.K. Chrugoo M.S., F.I.C.S.; C.L. Gupta M.S., M.Ch.;

Abstract: *Retrospective analysis of one hundred cases of advanced carcinoma of urinary bladder treated with surgery and radiotherapy was done and the success rate of various mode modalities adopted was analysed. Conservative external beam radiation therapy can give good local controls with bladder preservation but cannot be recommended as a curative single modality. Surgery remains the primary modality. Five year survival with local control is best in the early part of advancing disease and goes on decreasing with the progression in the stage and grade of the disease.*

Key words: *Bladder, Carcinoma, Radiotherapy, TUR.*

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Introduction

Urinary bladder carcinoma is one of the malignancies prevalent in various parts of the world[1]. Marked preponderance in males as compared to the females has been reported, incidence being 2-5 times more in males as compared to the females[2].

Incidence of this malignacy increases with age, particularly after the age of 60 years exposure to chemicals such as napthyl amine, xylene amine, dichlor bennzidie, auramie and magenta have been co-related with increased incidence[3]. Cigarette smoking has been reported to be one of the major causes of urinary bladder carcinoma in certain series.

Table-I:

Sex	:	M : F	
		90 : 10	
Age	-	Maximum after 6th decade	
Risk factors	-	Cigarette smoking	82%
Occupational dye exposure	-		4%
Alcoholics	-		60%

As far as the behaviour of the malignancy is concerned, the tumors are grouped into superficial bladder carcinoma and deep or advanced bladder carcinoma. The superficial urinary bladder carcinomas are those tumors which are confined to the mucosa and lamina propria of urinary bladder. Various treatment modalities have been used for these cancers. In the analysis only patients with deep or advanced malignancies were taken and this includes the presence of muscle infiltration with confinement to the urinary bladder, penetration through the muscularis into the perivesical soft tissue or involvement of regional lymph nodes. After diagnosis these patients were given external radiation and then followed up for five years. For them local control/failure have been analysed.

Methods & Observations

1. Patiet presentation: Most of the patients (80%) presented with haemeturia in our set up. 20% of the patients had bladder irritative symptoms.

Table-II:

Haemeturia	-	94%
Frequency of micturition	-	40%
Urgecy	-	34%
Clot retention	-	10%

Majority of the patients were anaemics. Cigarette smoking was the major risk factor in our study. Chief clinical presentation was haemeturia. Besides haemeturia bladder irritative symptoms were also significant. Transabdominal ultrasonography was helpful in 90% patients in detecting the advanced bladder malignancy. Intravenous urography is preferably performed prior to endoscopy to provide information relating to urothelium of upper tract as well as of urinary bladder. Urinary cytology was mainly positive in higher stage and higher grade malignancies. Cystopan endoscopy with TUR[4] (bladder tumor) remained the mainstay in the diagnoosis of urinary bladder carcinoma and establishing the state and grade.

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Table-III: Showing %age of diagnosis on Investigations

Transabdominal ultrasonography	-	90%
Intravenous urography	-	60%
Urinary cytology	-	84%- (grade III) 37% in (grade II)
Cystopanendoscopy	-	100%

These patients were then staged for their further treatment with radiation therapy.

Table-IV: Stage wise presentation

Stage		NO. of patients
B_1	-	25
B_2	-	48
C	-	12
D_1	-	10
D_2	-	5

Modalities of Treatment:- After initial cystoscopy and TUR, patients were subjected to external beam radiation therapy. Patients with stage B_1 & B_2 with grade II and grade III tumors are given localized field radiatioin by three folds with a dose of 66 gy/33#/6½ weeks by one anterior field and two posterior oblique fields. The radiation planning was done on treatment planning system and rectum and spinal cord were spared.

All patients with stage C and D were treated with initial dose of 40gy/20#/4 weeks by anteroposterior pelvic fields so as to include the regional lymph nodes in the treatment field after this patients further received 20gy/10#/2 weeks by three fields and the spinal cord is spared with beam direction radiation therapy.

Five of the patients have also received systemic chemotherapy with M-VAC regimen. They had regional lymph node involvement with bony metastasis. Drugs used are Methotreate Ooxorulicin, Vinblastine and cisplation. Doses and schedule for M-VAC regimon are as under:-

Doses (MG/M) Square and Schedule for M-VAC

Drugs	Day 1	Day 2	Day 15	Day 24
Methotrexate	30	—	30	30
Doxorulian	—	30	—	—
Vinblastive	—	3	3	3
Cisplation	—	70	—	—

Repeated every 28 days.

Patients were then evaluated for their local control as well as five year survival. Check cystopanendoscopy was done 3 monthly for initial one year, then six monthly for one year and then yearly for five years. Ultrasonography, chest X-ray, CT scan abdomen and pelvis depending upon the affordability of the patients was advised urinary cytology was also taken up for follow up.

Table	5 yrs. Survival	Local control	Recurrences
B_1	42%	48%	525
B_2	18%	30%	70%
C	8%	24%	76%
D_1 & D_2	Nil	Not acheved	

Discussion

In the present analysis it has been observed that the radiatioin therapy in combination with inital TUR gives excellent local control with urinary bladder preservation. Most of the patients recurred away from the original site. Herr and associates (1983) in their study have showed that most of the recurrences were not at the original site. In 10% of the patients multiple recurrences occured andin 15% of the patients there was progression of the disease. The largest series of Edinburg[5,6,7] docmented a complete remission in 45% in one year in all stage B to C patients. However the five year local control rates were 25% whereas significant overall survival has been noted[8]. In the Edinburg series the best predictor of both local control and survival viz a viz each stage was the grade of tumors. Both the C.R. and lasting local control rates were significantly higher in high grade lelsions but paradoxically the survival rates were worst in these patients because of distant metastasis. In our study also we have not been able to achieve higher survival rates in B_2, C.D stages however the local controls were significantly higher 30% & 24%.

Although ionising radiation has been used extensively in the treatment of urinary bladder carcinoma in Europe and U.K. but in USA surgery is the primary treatment modality however curative radiation is used for patients who either refuse surgery or are medically inoperable or have locally advanced disease unsuitable for salvage cystectomy. The advantage of radiation and chemotherapy is to preserve a functioning urinary bladder. The local recurrence rates 40%-70% and five year survival of 20%-40% have been reported after radiation therapy alone in stage B_1 & B_2[9].

Primary treatment with the intent to preserve a functioning urinary bladder remains an attractive alternative to radical cystectomy with continent urinary division but needs an improvement in the results with the use of bracy threapy using temporary implants and the local control can be raised to 70%-88% and five year survival can be raised to 55% to 73%[10,11].

In conclusion, for patients under going bladder preservation, conservative external radiation therapy can give good local controls with five year surivial however, it cannot be recommeded as curative single modality. The usefulness of partial cystectomy and urinary diversions after prior radiation can give better results, but as per the exhaustive study of parson[12] et al, overall 81% of patients with recurrent disease are unable to undergo cystectomy because of advanced disease; age, refusal or poor medical status resulting in an overestimation of survival in favour of salvage cystectomy. This holds true in our set up also.

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ANTI-CANCER DRUGS AND ANTI-RABIES VACCINE AVAILABLE

IMMUNOGLOBULIN A (IG A) IN BRONCHIAL WASHINGS OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Akhtar M.A.; Latief P.A.; Siddiqi Mushtaq; Dhobi G.N.

Abstract: Concentrations of immunoglobulin IgA were measured by radial immunodiffusion in serum and bronchioalveolar lavage of 21 patients with chronic obstructive airway disease and 5 control subjects. Most bronchial washings contained detectable amounts of IgA. Average concentrations of IgA was similar in bronchial washings from patients with chronic obstructive pulmonary disease (COPD) and control subjects.

It was cbcluded that recurrent bronchial infections in most patients with chronic obstructive pulmonary disease cannot be attributed to immunoglobulin deficiency in blood or in bronchial secretions and IgA is present in bronchial washingts in concentrations greater than can be explained by simple transudation from blood.

Key words: COPD, Immumoglobulins; Bronchial wastings.

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Introduction:

It is believed that immunoglobulins functions at mucosal surfaces as elsewhere, in defense against microbial invasion. Secretions of upper respiratory, gastrointestinal and genitourinary tracts are known to contain high concentrations of immunoglobulin A (IgA) which is present in unique secretory form[1]. Concentrations of immunoglobulin IgA have not been so extensively studied in secretions of lower respiratory tract and can be of paramount importance against recurrent bronchial infections[2].

We measured concentrations of IgA in bronchial washings obtained from patients with chronic obstructive pulmonary disease and control subjects.

Material and Methods:

21 patients with characteristic clinical and physiological features of chronic obstructive pulmonary disease were selected on basis of two criteria[1] severe chronic airway obstruction as manifested by one second forced expiratory volume (FEV_1) of less than 50% of forced vital capacity (FVC)[2], absence of other significant disease which could alter IgA profile. Five subjects were studied who had no symptoms, physical signs or radiographic evidence of chronic lung disease, had no history of frequent chest infections, had no evidence of any illness known to alter serum concentrations of immunoglobulins i.e., chronic infection, cirrhosis or collagen vascular disease, were scheduled for bronchoscopy for reasons unrelated to chronic lung disease.

Patients were premedicated with atropine sulfate and phenobarbitol. Phyranx and larynx were anesthetized with 1% lidocaine. Bronchial washings were obtained from each mainstem bronchus by introducing 5ml of 0.15ml sod. chloride[3].

Concentration of IgA was determined in bronchial washings and serum by radial immunodiffusion[4] on commercially available agar plates. Standadized serum was used as reference standard.

Results:

When classified by clinical and radiographic criteria 5 patients with chronic obstructive pulmonary disease were found to be predominantly emphysematous. Rest of patients had predominant chronic bronchitis. Results of pulmonary function tests confirmed the clinical impression of severe chronic airway obstruction (Table 1).

Examination of bronchi of all patients with chronic obstructive pulmonary disease revealed erythema and edema of bronchial mucosa. The bronchi of all control subjects were normal in appearance.

IgA was detected in bronchial washings and serum of all patients. Average IgA concentrations were not significantly different in washings from patients and control subjects when expressed as absolute concentration.

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Table-1: Lung Function tests in six patients with Chronic obstructive lung disease

FEV_1(ml)	FVC ml	FEV_1/FVC (%)	TLC
350	1260	28	4700
1320	2230	59	5260
470	1250	38	4610
520	1630	32	7050
440	1050	42	4600
1570	3090	51	5750

Discussion:

This study was undertaken to study concentration of IgA in bronchioalveolar lavage and serum of patients with chronic bronchitis and compared with concentrations in serum and bronchioalveolar lavage fluid of control subjects. The IgA of serum is structurally different from the secretory form of IgA. In the present study, IgA was detected with antibody to x-chain, a structural component common to the serum and secretary forms of IgA[5].

It is known that IgA is predominant immunoglobulin class in most external secretions[1], despite the relatively low concentrations of IgA in serum. These observations have led to the concept that IgA reaches external secretions not by simple diffusion from blood but by a specific secretory mechanism[6]. This concept has been reinforced by observations that most IgA in external secretions is present in a unique secretory form that appears to be locally synthesized by lymphoid cells located beneath epithelial surface[1]. The existence of a secretary mechanism for IgA is consistent with observations by George A et al[7] who had studied all three immunoglobulins in bronchial washings of patients with chronic obstructive lung disease as well as observations made by present writers.

Most of our patients have normal or increased concentrations of IgA in serum and bronchioalveolar lavage. It does not appear that recurrent respiratory tract infections in most of these patients are due to any quantitative immunoglobulin deficiency.

Table-2: IgA (ug/dl) Levels in patients/control subjects

S.No.	Patients with serum	Bronchioalveolar lavage
01.	16	35
02.	13	37
03.	8	22
04.	23	36
05.	40	56
06.	7	19
07.	14	26
08.	9	12
09.	16	24
10.	7	11
11.	12	19
12.	14	38
13.	28	34
14.	8	26
15.	9	18
16.	14	22
17.	16	31
18.	14	18
19.	15	25
20.	8	15
21.	31	28
	Mean±SD 15.35±8.30 P<.001	Mean±SD25.81±10.25 P<.001
Control Subjects		
01.	31	55
02.	28	36
03.	34	38
04.	16	28
05.	22	36
	Mean±SD 26.2 P<.025	Mean±SD 38.6±9.94 P<.025

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ROLE OF PLATELET AGGREGATION AND EFFECT OF ASPIRIN IN ISCHEMIC STROKES-A RANDOMIZED STUDY

Sheikh Mohammad Saleem, M.D., D.M.; Sonaullah Shah M.D.; Bashir Ahmad Shah M.D.; Gulam Nabi Dhobi M.D. Feroz Shaheen M.D.

Abstract: *A random cohort of 50 patients of occlusive cerebro vascular disease i.e., cerebral thrombosis and transient ischemic attacks (TIA's) were compared with 25 age and sex matched healthy normal controls to determine various platelet functions prior, 48 hours and two weeks after therapy with two different doses of aspirin i.e., 350mg and 700mg per day. 20 more patients were kept as control group without aspirin therapy and were followed in the same way to see whether the effect was not spontaneous one.*

Platelet aggregation was significantly increased in patients than normal healthy controls and more in older stroke patients with (P<.001). Aspirin in two different doses had a similar significant effect (P<.001)on regression of platelet aggregation in patients as well as normal healthy controls with maximum effect at48 hours of aspirin therapy. There was no significant spontaneous regression in platelet aggregation in patients of control group (P>.05). Thus we conclude that platelet aggregation is increased in both stroke patients (especialy elder patients) and older healthy normal controls. Low dose aspirin is as effective as high doses in regression of platelet aggregation in both patients and healthy controls with maximum effect at 48 hours of therapy. Platelet aggregation regression in stroke patientsis is not a spontaneous phenomenon.

Key words: *Aspirin, Cerebral thrombosis, Occlusive cerebro vascular, disease, Platelet aggregation, Transient ischemic attacks.*

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Introduction:

Stroke is defined as abrupt onset of a non-convulsive focal neurologic deficit. A TIA is manifested by a neurologic deficit lasting less than 24 hours[1]. Vascular diseases of nervous system rank first among all neurological diseases[2]. Cerebro vascular disease which predominates in middle and later years of life cause around 200,000 deaths in USA each year. These diseases are either ischemia-infarction (85-90%) or intracranial haemorrhage (10-15%)in western countries while haemorrhages constitute larger percentage in Asia[1]. In India stroke incidence is0.9-4.5% of all admissions and 9.2-30% of all neurologic admissions with occlusive strokes (57-82%) and haemorrhagic strokes (5.9-37.9%)[4]. In our State also ischemic strokes constituted 48.8% of all strokes[3].

The commonest causes of occlusive cerebro vascular disease are atherosclerosis, thromboembolism and cardiogenic embolism[1].

The platelets play major role in initiation of thrombus formation by adhesion, aggregation and coagulation of fibrin. In 40% of ischemic strokes no obvious source is detected or known[1]. There is increased platelet aggregation in ischemic cerebro-vascular disease patients reported by various authors[4,5].

A number of drugs had been used to reduce platelet aggregation in these patients i.e.,dipyridamole, sulfinpyrazone, clofibrate, hydroxychloroquine with variable results[6-11]. Aspirin and ticlopidine are now used commonly for this purpose. Aspirin has been widely studied invarious doses ranging from 30-1300mg per day, is least expensive and significantly reduces platelet aggregation in these patients and in normal persons. This is also used in secondary prevention of ischemic strokes[1,11]. Aspirin acts by acetylating the cyclo-oxygenase enzymes in platelets thus irreversibly inhibits formation of TXA2 which is platelet aggregating and vasoconstrictive and its effects last for 8 days[1].

The stydy undertaken to determine the following objectives as to our knowledge no such study was conducted till-date towards this aim in this part of world.

1. the level of platelet aggregation in occlusive cerebrovascular disease patients (cerebral thrombosis and TIA's) and in normal healthy controls.
2. the efect of two different doses of aspirin i.e. 350mg and 700mg per dayon platelet aggregation in cases

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as well as controls and

3. to see whether the decrease in platelet aggregation in patients is a spontaneous phenomenon.

Material and Methods:

Present study was conducted in random cohort of 70 occlusive cerebrovasular disease patients i.e., cerebral thrombosis and transient ischemic attacks and compared with 25 age,and sex matched healthy controls. The study was carried in three groups.

Group I: Comprised 50 patients who received aspirin in two different doses i.e., 25 patients received 350 mg per day and another 25 patients received 700mg per day.

Group II: 25 normal healthy controls who received two similar doses of aspirin as in group I i.e., 12 (350mg) and 13 (700mg) per day respectively.

Group III: Comprised 20 stroke patients who did not receive aspirin and acted (1) controls for group I and (2) to determine spontaneous fate of platelet aggregation.

The exclusion criteria for these patients taken for study were[2,4,5].

1. More than 72 hours of onset of stroke.
2. Atrial fibrillation, valvular heart disease and recent myocardial infarction.
3. Hyperlipidemia, diabetes, polycythemia, renal disease and venous thrombosis.
4. Drug ingestion in preceding 2 weeks i.e, aspirin, sulfinpyrazone, dipyridamole, quinine, nonsteroidal antiinflammatory agents, cyclophosphamide, clofibrate, phenothiazines, propanolol, methyldopa etc.
5. Bleeding diathesis, peptic ulcer disease and aspirin allergy.

The patients were diagnosed on the basis of history, clinical examination and computerized axial tomography of brain. All the patients and controls were divided into two age groups i.e. younger (≤ 40 years) and older >40 years. All cases and controls were subjected to:

i. Routine investigations i.e. complete blood counts, erythrocyte sedimentation rate, bleeding time, platelet count, platelet morphology on smear, packed cell volume, urine analysis, kidney function tests, blood sugar, lipidogram, chest skiagram and electrocardiogram.
ii. Specific investigation i.e. platelet aggregation which was done by O' Brien's[12] method using ADP at the time of admission at 48 hours and 2 weeks in all cases and controls. Platelet count was initally done on platelet rich plasma (P.R.P.) and then again after adding ADP 20ug in 0.1mg of the barbitone buffered saline. The difference between two platelet counts gave the number of platelets aggregated and then percentage platelet aggregability was calculated by formula:

$$\frac{\text{Initial platelet count - later platelet count}}{\text{initial platelet count}} \times 100$$

Observations:

In present study the ageof patientswho received aspirin ranged from 40-75 years (Mean±SD; 58.86±8.66) stroke patients in the control group ranged from 45-73 years (Mean±SD;59.13±8.18) and healthy normal controls from 42-75 years (Mean±SD 58.28±8.63). Out of 50 patients (M:F = 35:15), 40 (M.F. = 28:12) were having cereberal thrombosis and 10 (M:F = 7:3), had TIA's. Whereas out of 20 (M:F = 11:9) patients of control group, 14 (M:F = 8:6)had cereberal thrombosisand6 (M:F =4:2) had TIA's and out of 25 healthy normal controls 16 were males and 9 were females.

The mean percentage platelet aggregation in stroke patients and healthy controls before receiving aspirin were 60.80±7.75 and 51.35±5.87 respecively difference of which was statistically significant (P<0.001). There was no statistically significant difference (P>0.05) in mean percentage platelet aggregation in patients before aspirin therapy and patients of control group.

Platelet aggregation percentage of patients before receiving 350mg of aspirin and 48 hours after aspirin were 60.80±7.75 and 51.16±7.92 respecitvely which was statistically significant (P<.001), although there was no statistically significant (P>.05) decrease in platelet aggregation between 48 hours and 2 weeks of therapy. Similar results were observed with 700mg of aspirin therapy (Table-1)

Table-1: Platelet aggregation in patients before and after two different doses of aspirin.

Time interval	Dose of aspirin per day	Platelet aggregation (Patients) Mean±S.D	Difference of means	S.E.	t	P
0 hoursV/s 48 hours	350mg	60.80±7.75 V/S 51.16±9.92	9.64	2.22	9.34	<.001*
48 hours V/S 2 weeks	350 mg	61.16±7.92 V/S 50.54±7.93	0.62	2.24	0.28	>.005
0 hours V/S 48 hours	700mg	61.85±7.04 V/S 51.00±7.37	10.85	2.03	5.34	<.001*
48 hours V/S 2 weeks	700mg	51.00±7.37 V/S 49.73±7.51	1.27	2.10	0.60	>.05

S.E = Standard error
t = Student's 't' test
P = p value
* = Statistically significant

Similarlymean percentage platelet aggregation in healthy controls before350mg of aspirin per day and 48 hours after therapy were 51.35±5.87 and 41.19±5.54 respectively ($p<.001$) which was statistically significant, without any statistically significant ($P>.05$) difference in mean platelet aggregation between 48 hours and 2 weeks of therapy. Effects with 700mg of aspirin were also similar (Table-II). There was statistically significant difference in percentage platelet aggregation between patients and healthy controls before and after therapy with twodifferent doses of aspirin at all stages with P value ($P<.001$). There was no significant difference in effect between two different doses of aspirin in decreasing platelet aggregation ($p>0.05$) in both patients as well in controls (Fig. Ia, Ib).

In stroke patients of control group there was no statistically significant difference ($P>.05$) in mean percentage platelet aggregation between 0 hours and 48 hours and then 48 hours and 2 weeks of study (Table-III).

Table-II: Platelet aggregation in healthy controls before and after two different doses of aspirin

Time interval	Dose of aspirin per day	Platelet aggregation (Controls) Mean±S.D	Difference of means	S.E	t	P
0 hours V/S 48 hours	350mg	51.35±5.78 V/S 41.19±5.54	10.16	2.23	4.36	<.001*
48 hours V/S 2 weeks	350mg	41.19±5.54 V/S 40.18±5.28	1.01	2.20	0.46	>.05
0 hours V/S 48 hours	700mg	52.13±6.31 V/S 40.64±6.36	10.49	2.49	4.61	<.001*
48 hours V/S 2 weeks	700mg	40.64±6.36 V/S 39.77±6.04	0.87	2.43	0.36	>.05

S.E. = Standard error t = Students's 't' test
P = P value * = Statistically significant

Table-III: Platelet aggregation in patients of control group who did not receive aspiration at different time intervals

Time interval	Platelet aggregation Mean±S.D	Difference of means	S.E	t	P
0 hours V/s 48 hours	62.00±7.00 V/S 61.70±6.50	0.30	2.28	0.18	>.05*
48 hours V/S 2 weeks	61.70±6.50 V/S 61.30±6.35	0.40	2.13	0.21	>.05*

S.E = Standard error t = Student's't' test
P = P value * = Insignificant

Discussion:

The effect of different doses of aspirin on platelet aggregation in occulusive stroke patients have been studied widely. Our study in addition also shows platelet aggregation in normal healthy controls and effects of aspirin therapy in them. We also studied the platelet aggregation in occlusive stroke patients at different time intervals without aspirin therapy to know the spontaneous fate of platelet aggregatoin in them.

Platelet aggregation percentage was higher in older than in younger normal controls ($P<.001$) which was statistically significant. These findings were consistent with literature[5].There was no statistically significant difference in platelet aggregation ($P>.0.05$) between males and females which was in accordance with Patrignani et al[13].

Various workers have tried different doses of aspirin to see the effect in ischemic brain and found that they decrease platelet aggregation in all age groups and botrh sexes[14,15]. We also found that 350mg of aspirin was as effective as 700mg of aspirin with significant decrease in platelet aggregation ($p<0.001$) in healthy normal controls consistent with earlier studies[14-16]. These findings were seen in both sexes and in all groups with maximum effect at 48 hours of therapy which was in accordance with the earlier observations from various authors[17-18].

Similar observations were found in stroke patients who were put on similar doses of aspirin ($p<.001$) in all age groups and in either sex. These all findings were consistent with those reported in literature[2,4,15-16].

In case of stroke patients platelet aggregation percentage was significantly higher compared to normal controls (difference of mean±S.E-1.73 with $P<0.001$) consistent with study done by Gupta et al[2]. This reveals that patients are at higher risk of developing strokes. To know the spontaneous fate of ischemic brain while comparing the strokes patients in control group who did not receive aspirin and patients on aspirin therapy showed no statistically significant decrease in platelet aggregation at 48 hours or 2 weeks of study as compared to basal level ($P>.05$) revealing that decrease in platelet aggregation in stroke patients is not a spontaneous phenomenon as compared to patients on aspirin therapy, so it is the aspirin which has this effect which is in accordance with that observed by Dougherty et al (1979)[4].

Conclusion:

On the basis of this study we conclude that:

1. Platelet aggregation increases with age in normal healthy controls and in all occlusive stroke patients.

2. It is more in patients than in age and sex matched healthy controls.

3. Low doses of aspirin is as effective as high dose aspirin in regression of platelet aggregation in both patients and healthy controls with maximum effect at 48 hours of therapy.

4. Regression of platelet aggregation in patients is not spontaneous phenomenon but the effect of aspirin.

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PROFILE OF COMPOUND DEFECTS OF LEG AND FOOT IN KASHMIR - A RETRO-PROSPECTIVE STUDY

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Abstract: This study attempted to find out the clinico-pathological presentation and compare the outcome of the various reconstructive surgical procedures used to treat the compound defects of the leg and foot.

Fifty patients (39 males and 11 females) which included labourers (24%), students (24%); shopkeepers, farmers and office employees (12% each) were evaluated from June 1991 to June 1995 in this study.

The commonest site was upper one-third of leg (40%), followed by middle one-third (20%), hind foot (20%). The size of largest defect was 20 x 16 cms (range 5x3cms to 20x16cms). The causative factors were road traffic accident (20%), Fire arm injuries (20%), burns (14%), squamous cell carcinoma of the skin (8%), melanomas, trauma, radiation, neurotrophic ulcers, venous ulcers, sarcoma,diabetic gangrene, Ewing's tumor and osteomyelitis accounted for rest of the causative factors. The various surgical procedures carried out included. Gastrocnemius muscle flap (40%), Soleus muscle flap (20%), Cross leg flap (10%), Reverse post tibial artery flap (6%). In defects of heel and foot, the procedures used included Flexor digitorum brevis muscle flap in 8% and split skin thickness graft in (SSG) 10% of cases, who had an intact periosteum.

At follow-up 78% of cases showed excellent recovery and healing effect with no surgical complications. Most of the patients rehabilitated in their parent occupations.

Key words: Compound defects, leg and foot, muscle flap.

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Introduction:

Consequent to human mechanization and entry into scientific age, injury to the body architecture of lower limbs particularly leg and foot has become a very common occurrence. There is an increase in the frequency of lower extremity injuries in the civilian environment of high speed vehicles, sports injuries, gun-shot wounds. Other diverse causes that result into compound tissue defects of leg and foot include burn injuries, tumor resections (Kangri carcinoma, Marjolins ulcer, Venous ulcers, radionecrosis, neurotrophic ulcers. There are many more ulcers like diabetic, tubercular, atherosclerotic which may occassionally be the cause of compound defects of leg and foot. In these cases failure of healing have been common and as a short cut of these challenging defects till recently many advocated amputations. Whatever the etiological basis, the lower extremity defects in the form of exposed bone devoid of its periosteum are the most challenging problems for a reconstructive surgeon. In this study we have shown how legs previously doomed for amputation can be saved by repair of vessels, nerves or by reconstruction with various new flaps. Even the economical burden on hospitals is reduced to minimum and patients retain their parent work within a short period of time.

Material and Methods:

This was a retrospective and prospective study in which a total of fifty patients were included over a period of four years (from June 1991 to June 1995). The retrospective study included all the patients of compound defects of leg and foot encountered from June 1991 to June 1993. Their case files were studied in detail with respect to clinical history, investigations and treatment received including the reconstructive efforts if any undertaken. The prospective study included all the cases of compound defects of leg and foot from June 1993 to June 1995. Each case was selected for type of surgical intervention according to its presentation i.e. type and level of fracture, amount of soft tissue damage, condition of wound and bone and the neurovascular status of the limb. The profile of compound defects due to different causes, their clinical presentation, various modalities of treatment and the result of various procedures used in each case was recorded. The merits and demerits of each procedure was compared in this study.

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Treatment modalities:

Lower extremity skin defects with exposure of the deep tissues often involve extensive damage particularly arterial injury, which cause severe circulatory disturbances. Therefore in some patients with skin defects, the use of local flap or a muscle flap from the affected leg is accompanied by the contracture of knee and ankle joints[11]. Besides this the lower leg remains a difficult area to cover with a local flap. In order to prevent this complication, we used cross leg flap for the defects of lower leg and ankle. In this study we have performed medial Gastroenemius muscle flap in 40% of cases. These flaps are the work horses of the lower leg defects[12]. The medial Gastrocnemius cross leg flap has been helpful in situations where free tissue transfer was thought to carry an excessive risk. This flap offers a long narrow pedicle for maximum rotation. Thus it makes positioning of the leg more flexible.

We performed Soleus muscle flaps in the middle third of leg in 20% of cases. The advantages of soleus muscle is that it has an extensive blood supply which is an advantage not just for nutrition but adding as a "Venous Pump" too. This fact is strongly defended by Townsend PLG (1978) who described the soleus muscle as a useful and reliable flap particularly for closing the larger defects in middle and lower part of the leg[13].

Soft tissue coverage of the distal part of the leg and heel remains a difficult challenging and frustrating problem for the patients and surgeons.

The flexor digitorum brevis myocutaneous flap was used as a transposition flap for non-healing ulcers and the lesions of the heel (Malignant melanoma) by the Bostwick (1974), Shah A and Pandit S (1984). The authors mentioned above had used the flexor digitorum brevis muscle flap in smaller defects of the heel[14,15]. However, in our study we could cover the big defects of the posterior heel by the same muscles successfully.

Lastly we have used split thickness skin grafts (S.S.G.) to cover the smaller defects of the foot where periosteum was totally intact successfully, because there is comparatively larger supply of donor areas of S.S.G., and there is also comparative ease of harvesting.

Results:

During the period 1991-1995 total hospital admissions were 63465. Out of these, those admitted for lower extremity defects were 93, but those with compound defects of leg and foot were 50(0.07). Since the department of Plastic Surgery, Sher-i-Kashmir Institute of Medical Science, Srinagar, is the only referral centre for the entire valley. This figure aptly signifies the incidence of compound defects of leg and foot as seen in Kashmir Valey. In this study, the youngest patient was of 3 years and the oldest 60 years. Males predominated the study with male to female ratio of 3:5:1.

Higher incidence of compound defects was seen in labourers and students (24% each) (Table-2). Most common site of defect was seen in upper one-third of leg. 40% and the least common site was lower one-third of leg 10% (Table-3). Smallest sized defect was 5x3cms. and largest was 20x16cms. In 98% of cases joint status was normal and only in 2% of cases where osteomyelitis was pre-existing, joints were stiff. Distal neurovascular status was unaffected in 94% (47 of 50 cases) and only in 6% (3 of 50) cases the status was impeded.

Besides routine investigations like haemogram, serum chemistry, X-ray chest, urine analysis, some specific investigations were also performed like skiagram of leg and foot, histopathology of growth ad for swelling over the limb.

Various surgical procedures were carried-out in this study depending on the size and site of the defect as shown in table-5. The main post-operative complication was infection and necrosis of flap in 14% and 8% of cases respectively (table-6), while as no complications were seen in 78% of cases. Most of them got rehabilitated in their parent occupations.

Table-1: Age & Sex

Male	Female	Total	Ratio
39	11	50	3:5:1

Table-2: Occupation

Occupation	No.	Percentage.
Labourers	12	24
Students	12	24
Farmers	06	12
Shopkeepers	06	12
Office employees	06	12
House wives	05	10
Businessmen	01	02
Teachers	01	02
Sanitary workers	01	02

Table-3: Site of defect

Site of defect	No.	Percentage
Leg upper one-third	20	10
Middle one-third	10	20
Hind foot	10	20
Fore-foot	05	10
Lower one-third	05	10

Table-4: Cause of defect

Cause of defect	No.	Percentage
Road traffic accident	11	22
Bullet/fire arm injuries	11	22
Sq. cell carcinoma	04	08
Burns electric	04	08
Burns Kangri/Kerosene	03	06
Melanomas	03	06
Trauma (Gang-rivalry)	02	04
Radiation	02	04
Marjolin's ulcer	02	04
Neurotorphic ulcers	02	04
Venous ulcers	01	02
Sarcoma	01	02
Ewings tumour	01	02
Frost bite	01	02
Diabetic gangrene	01	02
Osteomyelitis	01	02

Table-5: Surgical procedures (Treatment modalities)

Type of surgical procedure	Site of defect	NO.	Perceptage.
Gastrocnemius Muscle flap	Upper 1/3rd of leg	20	40
Soleus muscle	Middle 1/3rd flap of leg	10	20
Cross leg flap	Lower 1/3rd of leg	05	10
Flexor digitorum brevis	Heel defects	04	08
Reverse post-tibial artery	Foot defects	03	06
Rotation flap	Foot	03	06
S.S.G.	Smaller defects of foot	05	10

Table-6: Post-operative complications

Post-operative	No.	Percentage.
Infection	07	14
Partial flap necrosis	02	04
Total necrosis	02	04
Total	11	22

Discussion

This study of 50 patients seen over a period of four years (1991-1995) has revealed relatively high incidence (0.07%) of compound defects of leg and foot. This can directly be attributed to the increase in traffic accidents and the higher range of bullet and blast injuries as a sequale to the present turmoil in the Kashmir Valley. Maximum patients (53%) were seen in the second and fourth decade of life with a male to female ratio of 3.54:1. Leg and foot defects as a sequalae to bullet and blast injuries were found in a younger age group from 20-30 years while those due to various road accidents were found in a relatively older age group (35 years). The most out-going community labourers and students were affected most (24%), while as less out-going people like farmers and house-wives were the least sufferers. The most common site of involvement was upper one-third of leg in 20 patients (40%) followed by middle one-third leg in 10(20%) of cases. Our data is more or less similar to that oof Kujima T[1] and Jones RE[2]. We have observed relatively larger sized defects 20x16cms and the average being 9x5cms. which does not correlate with the data proovided by other authors like Barclay[3]. Cardoso et al. The main causative factors of leg and foot defects in our study were due to bullet and fire arm injuuries 22% and road traffic accidents 22%, followed by electric/Kangri burns, squamous cell carcinoma of skin and malignant melanoma in 8% and 6% respecively. Our data is contrary to that of McHuge and Tolhurst, who reported industrial injuries, vehicular accidents and fall from height being the main causative agents[4,5].

The pre-existing systemic diseases in our cases were diabetes mellitus, squamous cell carcinoma, varicosity of veins and tuberculosis. These causes simulate with the causes in the studies of Hamilton (1854)[6], Macomber and Roubin (1947)[7] and Stark (1951)[8].

In majority of our cases, the joint status, distal neurovascular status and nutritional stastus was ranging from unaffected to good respectively. This simulates with the studies of authors like Chabda PS (1990)[9], and Brown (1990)[10].

In the present study, we observed minimal complications in the form of infection (14%) partial and total necrosis was seen in 4% of cases each, while as 78% of patients remained free of any complication post-operatively. However, majority of our cases had grossly mutilated and highly infected wounds as witnessed in road traffic accidents and various fire arm/blast injuries. Patients who developed post-operative complications a second sitting surgical intervention was undertaken with successful outcome.

Conclusion:

Our experience with the medial gastrocnemius, soleus muscle flap and cross leg flap is presented in this series. Our study had proved the excellent utility to these muscle flaps in the defects of leg and foot. Flexor digitorum brevis flap was used to cover big defects of heel and foot in our study and SSG to cover the smaller defects of foot successfully in intact periosteun. We found the above mentioned methods are simple and reliable to cover compound defects in upper middle and lower third of leg and foot. These methods in our experience have proven to be a promising technique and give us good reason to continue using it in order to reduce the patients stay in hospital and rehabilitate the patient in the shortest possible time to make him fit for his routine day to day work and earn his livelihood.

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ROLE OF THERAPEUTIC EXERCISES AND REHABILITATIVE PROCEDURES IN BRACHIAL PLEXUS INJURIES

Ali Mohammad Buhroo M.S.; Nissar Ahmad Khan M.D.; Shakeel Ahmad Mir.

Abstract: *This study was conducted on 29 patients of either sex and of any age with brachial plexus injuries, managed conservatively and followed for more than 2 years. 6 cases had bilateral brachail plexus injuries. Most of the patients had traction type of trauma usually due to road traffic accidents and torture. The prognosis in these cases was good on conservative management. Type III injuries didnot recover completely and had residual disability. Hence it is concluded that early intensive therapeutic exercises and other rehibilitative procedures are very much essential in all types of brachail plexus injuries leading to complete recovery in type I and type II injuries and preventing complications like contractures, deformity,wasting and anaesthetic sores in type III injuries, for their better management by reconstructive procedures later on.*

Brachail plexus injuries are of special interest as they lead to suddent paralysis of upper limbs making a person to lose his activity of dialy living (ADL) completely with emotional breakdown. Hand being highly specialized sensory-motor organ, performing delicate and complex movements and has highly specialised discriminative and stereognostic function,needs specialised rehabilitative training programmes for resotration of such functions. This is achieved by sensory re-education.

Key words: *Brachial Plexus injuries, Rehabilitative procedures*

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Introduction:

Brachial plexus injuries are becoming more frequent because of increase in road traffic accidents. Invariably these are closed traction injuries resulting from head being forced laterally at the moment of impact. Other causes include torture induced, post-surgical, post-irradiation injuries and fall etc. Open injuries are due to gun-shot,knife cut or missile blasts.In neonates birth trauma to brachial plexus will lead to upper root or lower root injury.Brachial plexus is concerned with nerve supply to upper limbs, especially hands.The hands are highly developed and specialised sensory organs having stereognostic and discriminative functions and performing the most complex and intricate, integrated and well ,co-ordinated, skillful and purposeful movements of daily living. The sudden loss of such function from brachial plexus injury leaves a person jobless with emotional break-down[1].

Brachial plexus lesions could be partial or complete. For established complete lesions the choice of treatment is between three alternatives;to leave the limb alone, to undertake extensive surgical reconstruction by primary repair, delayed primary repair or secondary repair, followed by extensive rehabilitative approach, started as early as possible.

Despite recent work on axon regeneration, there are no proven measure or procedures that will hasten the onset of regeneration or accelerate the growth of regenerating axons along the nerve sheath[2]. Treatment is, therefore, confined to prevention of those complications at periphery that will threaten the restoration of function in structures that will ultimately be reinervated. Bearing in mind the co-existing injuries to other structures, the treatment should be started as early as possible for these injuries.

The main objectives of rehabilitative and therapeutic procedures of such injuries are; to keep the denervated muscles, joints, peri-articular tissue and skin in optimal functional status and prevention of deformities pending recovery and reinervation. After the reappearance of voluntary movement the emphasis changes to remedial training directed to increasing the range,power and quality of integrated movement and the range, quality of discriminative sensibility and stereognostic functions.

In our set-up the branchial plexus injuries are common among young males mainly due to road traffic accidents, torture induced and blast injuries. Hence this study was conducted on patients of brachial plexus injuries who have been given a thorough trial of rehabilitative and therapeutic treatment and were

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followed for six months to three years.

Material and Methods

Patients of brachial plelxus injuries attending the PMR department of SKIMS and of all age groups and of either sex, whether operated or not, were studied. Patients with birth injury in neonates, postirradiation and malignant infiltration in neck and due to degnerative joint disease involving brachial plexus were excluded. A detailed history with thorough clinical examination with a record of neurological involvement i.e. motor, sensory and autonomic deficit were recorded. Muscle power grading, sensory charts, self assessment chartsand final functional assessment were recorded[3].

Investigation included routine haemogram, urine examination, X-ray chest, neck and shoulder, NCV and EMG; CT scaning or cervical myelography was done in few cases. Few patients were admitted for management but most of these patients attended for specialised treatment on OPD basis.

Management:

Treatment was mainly aimed at emotional support, care of denervated muscles, peri-articular tissues, joints and insensitive skin. This was achieved by various rehabilitative and therapeutic procedures to keep the paralysed limb in optimal functional position, thus preventing development of contractures and deformity of joints[4].

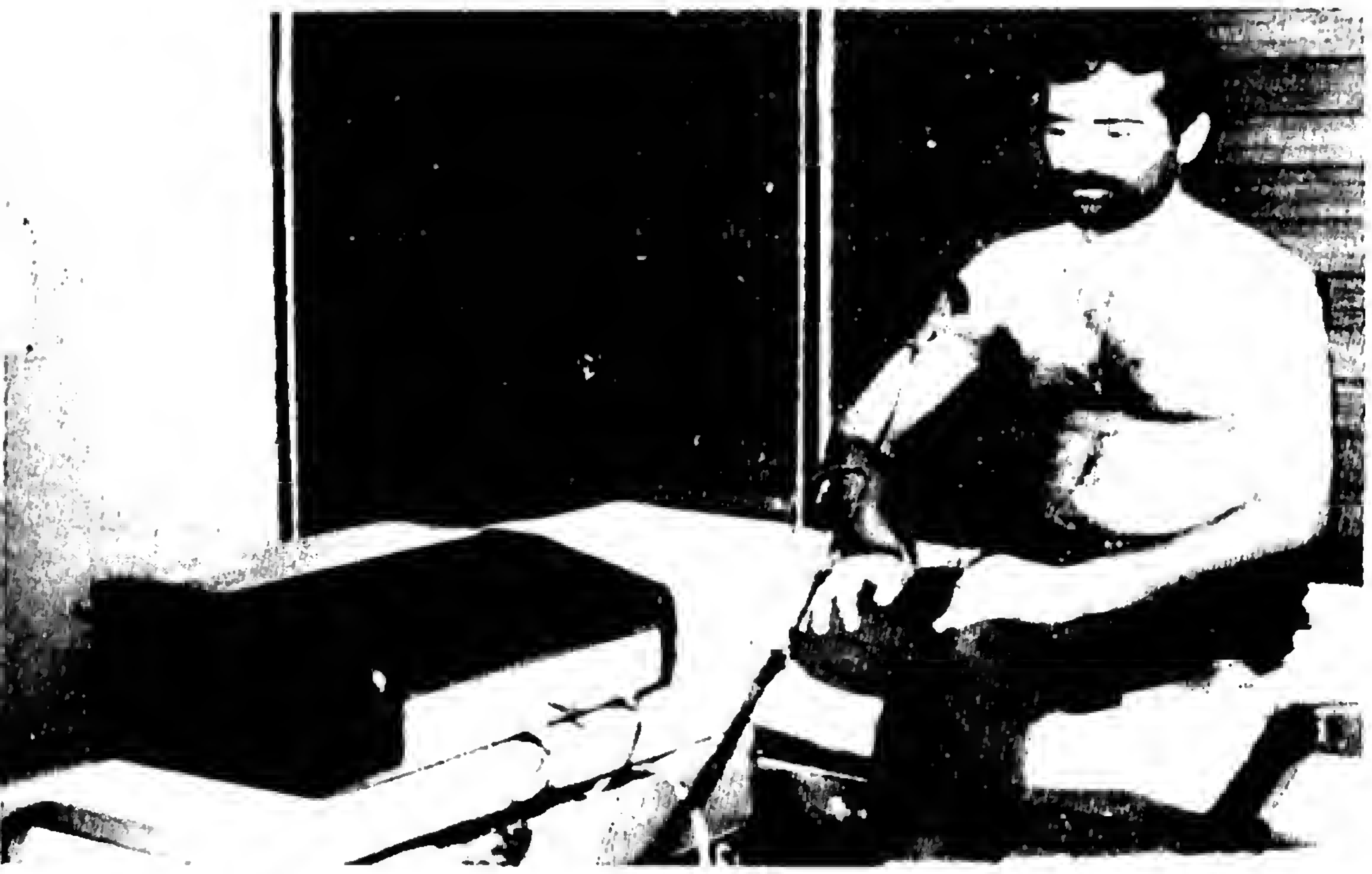

Fig.I. Patient of Brachial Plexus injury receiving electrotherapy

Careof Denervated Muscles:

These were protected against cold and heat exposures, minor trauma and over-stretching by gravity. The muscles were kept in normal physiological length to prevent vascular and lymphatic stasis, contractures, joint stiffness and ankylosis. Procedures directed to achieve above goals were warmth, massage and movements, bandaging, TENS (Fig.2) and electro-therapy, (Fig-I) pneumotherapy, ultrasonic therapy, hydro-therapy and splints and other mechanical devices[5]. Splints and mechanical devices were used to give rest to the paralysed muscles and joints, preventing over streching and shortening and thus avoiding contracture formation and deformity.

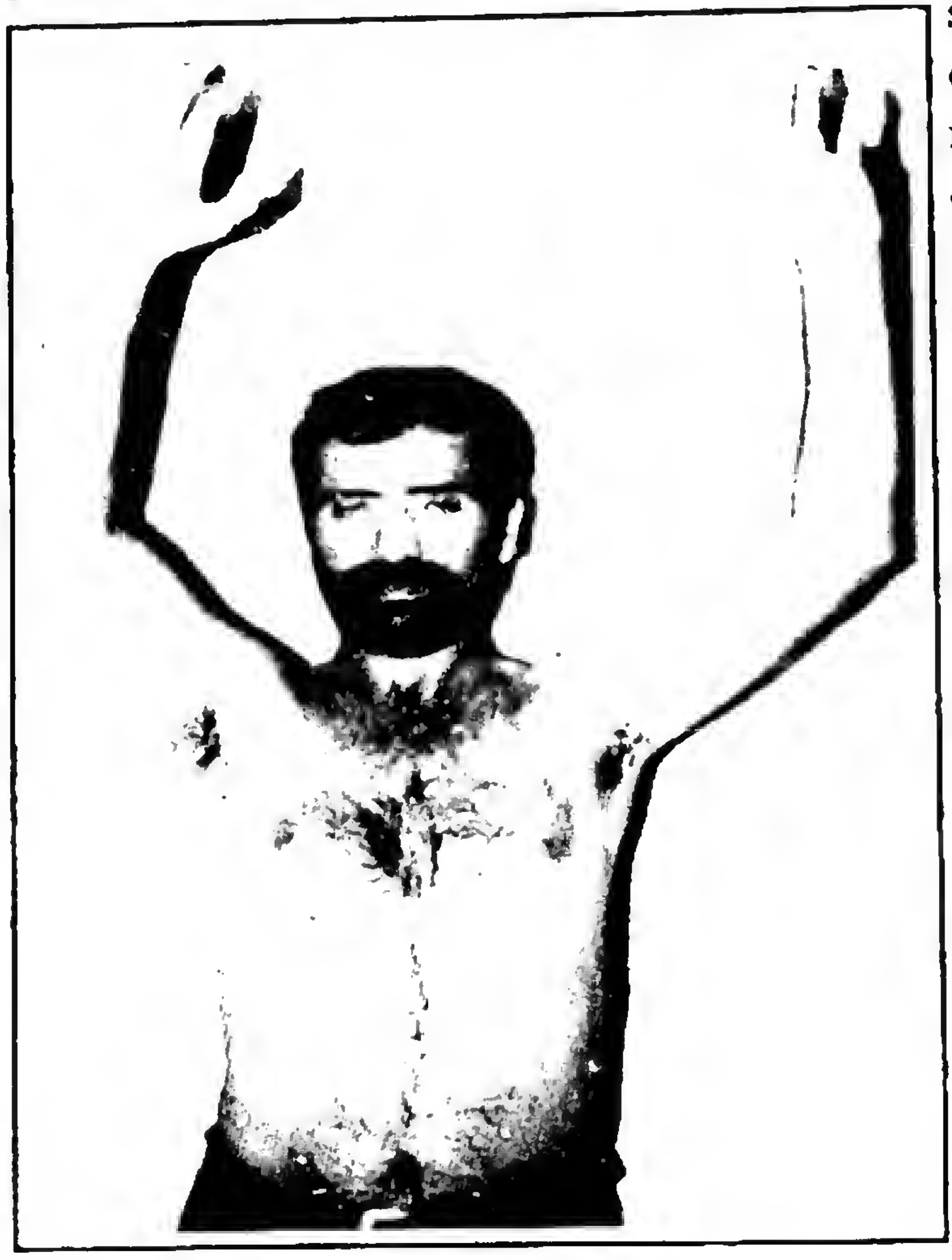

Fig.2. Patient of B/C brachial Plexus injury recovered fully.

These splints and other devices were detechable and dynamic to allow exercises and other therapeutic procedures to be given regularly and to prevent complications of continued immobilization.

Care of Joints and Periarticular Tissues:

The insensitive joints and ligaments and other sorrounding tissues were maintained in full functional position by daily and regular ROM exercices and dynamic detachable splints. These splints protected insensitive joint systems from external injuries.

Care of Skin:

Patients were asked not to handle hot and sharp objects and avoid use of hot water bottles, take care of nails and avoid exposure to cold and use of incorrect splints.

Sesnory re-education:

This was necessary to learn to interpret the altered profile of impulses reaching his/her conscious level after the injured limb is stimulated by stimulating the finger tips by erasor edge of pencil from proximal to distal area in early phase and involved repetitive object identification to learn stereognosis in late phase of recovery[6].

Results:

29 patients ranging between age of 15-60 years with maximum number of patients between 15-30 years (17) were studied. 4 patients were lost to follow-up after one year and were excluded from final results. Sex ratio was 6:1 (male/female).

The high incidence in younger age group was because of torture induced injury in this age group.

Type of Injury: (Table-1)

There were 6 bilateral brachial plexus injuries mainly due to the tórture by tying their both hands from behind the chest wall and hanging them from the ro of. 13 patients had complete brachial plexus injuries. 9 had lower brachial plexus involvement and one had upper brachial plexus injury. The left side was involved in 16 patients and right side in 7 patients.

Table-1:

Type of injury	No. of Patients Left side	 Rt.Side	 B/L
Upper brachail plexus	-	1	-
Lower brachial plexus	7	2	-
Complete brachail plexus	9	4	6

Nature of Trauma: (Table-2)

10patients had road traffic accidents, 8 patients had torture,6 patients had fall from tree/house, two each were due to fire arm and blast injuries. One case was due to surgery on neck.

Table-2:

Natureof Injury	No. of patients
Road traffic accident	10
Torture	8
Fall	06
Fire arm injury	02
Blast injury	02
Surgery	01

Neurodeficit:

All the patients had both sensory and motor deficit. The patients were divided into four groups according to motor power. Maximum number of patients i.e. 14 had grade IIIto IV power with partial sensory loss; they had usually traction type of injury with neuropraxia only. 4 patients had grade 0 to 1 power, 9 patients had grade I to II and two patients had II to III power.

Follow Up: (Table-III)

Maximum number of patients were followed upto one year and few patients beyond one year. 16 patients with type I injury (neuropraxia) needed follow up upto six months to one year only. The intensive therapeutic and rehabilitative re-training programme and exercises led to the recovery of these patients in all parameters, i.e. sensory, motor and stereognostic, by six months in ten patients. Another six patients showed complete recovery by one year and were back to their job. None of these patients developed any contracture, deformity or any other sensory problem (Fif-2).

9 patients with type II injury (Table-III) showed some sings of recovery by the end of three months and four patients recovered completely at the end of six months. At the end of one year six patients had recovered fully

FOLLOW UP

TABLE III

Type of injury	No. of patients	3 months	6 Months	1 years	Beyond 1 year
I.	16	All patients showed signs of partial recovery in terms of sensory and motor deficit	10 pts. recovered complete 6 patients showed partial recovery	All recovered completely	Back to their job
II.	9	Improved partially in terms of motore and sensory deficit	4 patients showed complete recovery 2 patients showed partial recovery 3 patients showed little improvement	6 patients showed complete recovery 3 patients showed little recovery	8 patients back to the job after complete 1 patient persisted with wrist drop.
III.	4	No improvement 3 pts. Signs of improvement In one patien	No improvement in 3 patients One showed more improvement	No improvment In 3 patients 1 patient recovered	No Improvement showed same deficit one patient back to job.

without any residual deformity but three patients had partially recovered. Out of these three patients, two patients showed complete recovery beyond one year and one patient persisted with wrist drop. In type III injuries (neurotmesis) four patients showed no improvement at the end of three months but they were given intensive rehabilitative programmes and various mechanical devices and splints to prevent contractures and joint deformity. Only one patient out of this group started showing improvement partially at the end of six months. The remaining three patients did not show any improvement at the of one year, these patients with partial recovery were using orthotic device for weak joints. These three patients were lost to follow up after 1½ years.

The final results of these29 patients (Table-IV) showed that 25 patients recovered fully without any residual disability, four patients had partial recovery and were lost to followup.

Discussion:

This study was done on 29 patients to emphasize the role of various therapeutic and rehabilitative training programmes in all types of brachial plexus injuries. Patients with type III brachail plexus injuries with bad prognosis also need to be rehabilitated in the early states for various reconstructive surgical procedures, amputations or orthodesis. Even after surgery retraining programmes are necessary for proper functioning of the stump and use of prosthesis.

The maximum number of patients in the present series were young adult males between age of 15-30 years. They had usually traction type of injurie with 6 patients having bilateral involvement. The high incidence in this age group was because of torture induced injuries and road traffic accidents. The left side was involved in 16 patients. The neurodeficit varied from Grade 0 to 1 motor power to Grade III-IV in maximum number of patients[14]. The role of initial conservative treatment with intensive rehabilitation has also been emphasised by A.O. Rensford et al[7] (1977) in their 10 years follow up study of 20 cases with brachail plexus injuries. Seven cases in their study had no surgical treatment. Out of 13 amputees, only two were true prosthetic users having dominant limb involvement. They concluded that surgical procedures should be delayed upto one year in all cases when no further recovery is possible and then only amputation can be done if the limb is flail and non-dominant, preventing spporting activities and causing repulsion. In 1944 Henerey advocated extensive surgical repair for complete brachial plexus injuries followed by early rehabilitative training. Yoman & Sedden in 1961 in their series of 36 patients in whom16 had amputation, 8 had various reconstructive procedures and 12 had no opertive procedures, who were managed conservatively only and concluded that amputation with orthodesis offered better results than either surgical or non-surgical treatment. Sedon in 1972 had seen near total recovery in a boy with complete brachial plexus lesion of poor prognoosis. Wynn Parry (1974) in a series of 23 patients with complete brachial plexus injury, had 14 patients with amputation and orthodesis within six months of their injury. 10 returned to their work within one year. Wynn Parry (1981) had described a patient with a total brachial plexus injury in continuity whose sensory recognition time nearly approached normal within 18 months after total denervation.

FINAL ASSESSMENT TABLE IV

No. of pts.	Recovered fully	Partially recovered	Little improvement
29	25	01	03

In our follow up of 29 patients type I and type II injuries had better prognosis and recovered fully by six months to one year without any complications of paralysis i.e. joint stiffness, contracture or deformity or pressure sores. All patients returned to their job by the end of one year. Four patients with type III injury were also managed by various rehabilitative procedures for maintaining their joints and periarticular tissues in normal physiological status, pending recovery or reconstructive procedures. This is very important for their future rehabilitation in terms of using prosthesis or making them one handed.

Conclusion:

Brachial plexus injuries of type I to type III need intensive rehabilitative training and therapeutic approach for their better management. Type I and type II injuries have excellent prognosis, without surgical intervention, if managed properly at an early stage. Various therapeutic modalities and exercises will lead to proper recovery without any complications like wasting, contractures, joint stiffness and anaesthetic sores. Sensory reeduction will lead to proper functioning of hand.

Type III injuries, before surgical intervetnion, also need rehabilitation for keeping their muscles and peri-articular tissues in near normal physiological status. Even after surgery such injuries need contineous supervision in rehabilitation department. In this study we have mostly come across with traction type of brachial plexus injuries which recovered completely in all parameters by various rehabilitative procedures. Hence it is emphasised that management of nerve injuries as a whole needs a team approach consisting of rehabilitation specialist, physiotherapist, occupational therapist and neurosurgeon/

orthopaedic surgeon or the list.

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"A COMPARATIVE STUDY OF TWO ANTIEMETICS: DROPERIDOL AND GRANISETRON IN THE PREVENTION OF POST ANAESTHESIA NAUSEA AND VOMITING"

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Abstract: *A prospective, placebo controlled, randomized double blind study was undertaken to evaluate the effects of Droperidol and Granisetron in the prevention of post-anaesthesia nausea and vomiting 45 patients divided into three groups of 15 patients each were administered placebo or Inj. Droperidol 2.5 mg. I.V. or Inj. Granisetron 3mg I.V. just before induction of anaesthesia. The incidenceof nausea and vomiting in the three groups was compared and it was evaluated from the study that only 6.66% of vomiting, 6.66% of nausea was observed in the granisetron group, while as 26.66% of vomiting, 20.01% of nausea was seen in droperidol group and in the placebo group vomiting occurred in 53.33% of patients and 20.01 of patients had nausea in the post operative period.*

Key words: *Nausea, Vomiting,Post-anaesthesia, Droperidol, Granisetron.*

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Introduction:

Nausea and vomiting are the two most common distressing symptoms after general anaesthesia. Persistent vomiting in the post-operative period can result in electrolyte imbalance,longer stay in the recovery room, bleeding from the operative site and increased risk of aspiration. With the availability of new antiemetic drugs, the incidence of the said complications can be reduced dramatically. Recently Granisetron a selective 5 hydroxy tryptamine type $3(5HT_3)$ receptor antagonist has been used for the prevention of post-anaesthesia nausea and vomiting. Antiementics like antihistamines, butyrophenones and dopamine receptor anatagonists are used but these have undersirable side effects like dysphoria, dry mouth, hypotension and extrapyramidal symptoms.

Material and Methods:

We studied 45 patients of ASA I and II of both sexes between the age of 25 and 60 years who had to undergo general anaesthesia for major general surgery, plastic surgery and urological surgery. The drugs under study were Inj. Droperidol 2.5 mg and In. Granisetron 3mg both by intravenous route. The patients were divided into three groups of 15 each and Group A received Distilled water injection 3ml as placebo. Group B received Inj. Droperidol 2.5 mg I.V and group C received Inj. Granisetron 3mg I.V just before inductionn of anesthesia. The induction of anaesthesia in all the patients was started with preoxygeneation, Inj. Buprenorphine 3-6ug/kg body weight, Inj. Thiopentone 4-5mg/kg body weight I.V and succinylcholine 2mg/kg to facilitate endotracheal intubation. Anaesthesia was then maintained with N_2O and oxygen and pancuronium bromide 80ug/kg body weight. The patients were ventilated taking care not to overinflate the lungs. After the end of surgery, the patients were extubated and shifted to the recovery room for at least half an hour. The episodes of vomiting and nausea were observed for first 24 hours in the post-operative period and scoring was done. Score zero (O) meant no vomiting. Score one (1) meant only nausea and score two (2) meant nausea and vomiting.

Results:

The groups were comparable with regard to demographic data, type and duration of surgical procedure (table-1).

Table-1: Characteristics of patients.

No. of patients	Group A Placebo (15)	Group B (15)	Group C (15)
Age (years)	43±6	42±4	36±3
Sex (M/F)	7,8	6,9	4,11
Operating time (minutes)	84±11	98±10	87±14
Surgery (General, Plastic, Urology)	7,2,6	8,4,3	6,5,4

The incidence of nausea was 26.66% (score 1) and vomiting (score 2) was 53.33% while as no nausea and no vomiting (score 0) was 20.01% in the group-A patients

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(placebo). The incidence of nausea in group-B was 20.01% (score 1). Vomiting 26.60% (score 2) and no nausea and no vomiting (score 0) was 53.33%. While as in the Granisetron group (Group-C), the incidence of nausea was 6.66%, (score 1), vomiting (score 2) was 6.66% while as no nausea and no vomiting (score 0) was 87.68% (Table 2).

Table-2:

		Scrore 0 No nausea/ No vomiting	Score 1 Only nausea	Score 2 Only vomiting
Group A	Placebo 15 pts.	3 (20.01%)	4 (26.66%)	8 (53.33%)
Group B	Droperidol 15 pts.	8 (53.33%)	3 (20.01%)	4 (26.66%)
Group C	Granisetron 15pts.	13 (87.68%)	1 (6.66%)	1 (6.66%)

Discussion:

This study was conducted to answer two questions i.e. is an antiemetic necessary in association with general anaesthesia and if so, which is the most effective antiemetic that should be used to prevent post-operative nausea and vomiting. In our study, vomiting was usually in the early post-operative period and in the placebo group an incidence of 53.33% is unacceptably high as it is not only uncomfortable and inconvenient for the patient, but also poses the risk of aspiration of gastric contents when protective reflexes are depressed due to the residual effect of anaesthetic drugs.

The two antiemetics studied certainly reduce the incidence of nausea and vomiting. Statistical analysis shows that droperidol is less effective then Granisetron. Many different antiemetics like prochlorperazine, metoclopramide, cyclizine, atropine and hyoscine which are used toprevent post-operative nausea and vomiting are less effective then Droperidol and Granisetron and have side effects like hypotension, bradycardia or tachycardia, dry mouth, sedation and extrapyramidal symptoms.

Droperidol is a potent neuroleptic with antiemetic property. Clinical studies have shown it to be superior to Metoclopramide and Domperidone. However, when large doses of droperidol are used, delayed emergence, drowsiness and extrapyramidal signs may occur.

$5HT_3$ antagonist drugs are a major advance in the management of post-operative nausea and vomiting. These drugs lack the sedative and dysphoric side effects associated with high doses of metoclopromide. Granisetron is a selective antagonist of serotonin at the $5HT_3$ receptor with antiemetic effects against cisplatin induced nausea and vomiting.[6]

Our results indicated that granisetron has a potent antiemetic effect on post-operative nausea and vomiting. Although the precise mechanism of Granisetron in the prevention of post-operative emesis remains unclear, it is possible that granisetronmay act at the area postrema and the nucleus tractus so litarius which contains a number of $5HT_3$ receptors in the small intestine. In our study we used 60ug/kg body weight I.V of Granisetron (3mg I.V.) because it is known that effective doses of Granisetron are between40to 80ug/kg I.V for the treatment of cancer therapy induced nausea and vomiting.[10]

No adverse effects were observed in either the droperidol or the granisetron groups in the present study.

Many factors influence the incidence of nausea and vomiting after anaesthesia and surgery. They include thiopentone, methohexitone, etomidate, nitrous-oxide isoflurance, enflurane, halothane; although propofol is considered to have antiemetic action[9].

Muscle relaxants as such do not cause nausea and vomiting but neostigmine is known to increase muscle tone and may cause nausea. Opioids which are used extensively during, anaesthesia stimulate nausea and vomiting by an action on the chemoreceptor trigger zone in the area postrema.Adult women are 2-4 times more likely to suffer nausea and vomiting in the post-operative period. Obesity appears to increase the risk of post-operative nausea and vomiting. Post-operative factors like pain, mobility, hypotension and hypoxaemia can also result in post-operative nausea and vomiting. In conclusion, the present study suggests that administration of Granisetron is superior to Droperidol in the long term prevention of post-operative nausea and vomiting after anaesthesia.

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LEUCOCYTIC COUNT IN ACUTE EPIDIDYMO - ORCHITIS

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Abstract: Acute epididimoorchitis is a known cause of loss of work. If left alone, it can lead to abscess formation, testicular infarcts, infertility and to chronic testicular pain. Fifty patients were entered into the study; blood sample was taken for complete blood count, and mid stream urine analysis and culture was done aerobicaly on MaConky agar. Culture for Chlamydia was not available. Thirty one patients (62%) had leucocytosis with white blood cell count $16.0 \pm 5.0 \times 10^9$ *while in nineteen patients (38%) it was* $7.8 \pm 1.2 \times 10^9$. *Firty six patients had pyuria of more then 5 pus cells. There was no significant difference between the number of pus cells in urine with Leucocytosis and those with normal white blood cells. Hence, the presence of leucocytosis or pyuria did not predict a concomitant urinary tract infection in the study. Moreover, the urinary tract infection appeared to be evenly spread among all the age groups.*

Key words: Epididymo-orchitis, Leucocytosis, Pyuria.

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Introduction:

Acute epididymitis is a major cause of loss of work. In practice, it accounts for about 10% of out patient attendence and over 3% of male urological admissions. Complications from this disease include abscess formation, testicular infarction, infertility and development of chronic testicular pain. In adolescents and young adults, a major and important differential diagnosis is torsion of testis.

Early and accurate diagnosis of acute epididymitis is essential. Unfortunately, the cause of this condition has remained controversial largely because of difficulty in the isolation of non bacterial pathogens involved in some cases. Workers in Europe and North America[1-3] reported that patients with acute epididymitis fell into two groupus. Patients above the age of 45 years tend to have associated coliform urinary infection, with or without bladder outflow obstruction. Below this age, epididymitis was said to be associated with sexually transmitted disease, with chlamydia infection predominating. In absence of positive cultures, therapy was selected to reflect this pattern of infection[1].

There is little information regarding the causation of Acute epididymitis in the tropics, wholesale extrapolation of findings from Europe and America may be misleading. In view of this short-coming, a prospective study was designed to define the aetiology of acute epididymitis in a group of men that presented to the Department of Urology ASCOMS & Hospital, Sidhra, Jammu.

Patients and Method:

A consecutive series of men that presented to out patient department with symptoms and signs of acute epididymitis were entered into study. Most of the patients were reffered from Dispensaries and most had received antibiotics before referral.

At the first visit, a full physical examination was done. Blood was taken for complete blood count (CBC) including differential white cell count. A full examinatioin of midstream specimen of urine was made. Culture was done aerobically on MC Conkey agar. Urethral swabs were taken in men with a history of uretheral discharge. Culture for chlamydia was not available in our hospital during the period of this study.

Results:

The study spanned eighteen months period between January 1998 and July 1999. Fifty men were entered into the study. Their ages ranged from13 to 80 years (mean 34.7); 36 patients were aged less than 40 years and 14 were 40 years or more. The right testis was involved in 29 cases and the left testis in 21. No patient proved to have testicular torsion. Twenty nine cases presented with a temperature of more than 38°C and were admitted for parenteral antibiotics. Three patients gave a history of Urethral discharge; eight had symptoms of urinary tract infection among whom were three men aged more than 60 years with prostatic enlargement.

Thirty one cases (62%) had leucocytosis with a WBC count of $16.0 \pm 1.2 \times 10^9$. Forty six patients had pyuria of

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more than 5 pus cells per high power field but there was no significant difference between the number of pus cells in urine of men with leucocytosis (16±10) and those with normal WBC (13±111), p>0.05. The MSU of thirteen case were positive; 10 grew coliform organisms and pseudomonas was cultured in[3]. Of the men with positive urine cultures, 11 were under the age of 40 years, 7 had pyrexia of greater than 38°C, but only two gave a history of urinary tract infection. All three urethral swabs were sterile.

Hence the presence of pyrexia, leucocytosis or pyuria did not predict a concomitant urinary tract infection in this study. Moreover, the urinary tract infection appeared to be evenly spread among all age groups.

Discussions:

The treatment of acute epididymitis can sometimes be very difficult. Often the inflammation spreads to the adjacent testicle. On the other hand, the epididymal oedema may compress the testicular blood vessels and urgent epididymotomy will be required to save the testis. Appropriate therapy requires knowledge of the causative micro-organism. In this there is lot of controversy.

Previous workers [1,3] had suggested that patients with acute epididymitis fell into two distinct groups. Those above the age of forty five were thought to have a degree of bladder neck obstruction and usually have bacterial cause for their disease. Younger men tend to have sterile urine cultures and a veneral aetiology. The findings in this study are at variance with this observation. The majority of our patients with positive urine cultures were below the age of forty. Moreover, the three men with obstructive voiding symptoms had sterile urine. It may be argued that previous antibiotic may have influenced the outcome of urine cultures in this study. However, virtually all the patients received prior treatment and any adverse effect would be uniform. The experience in Leeds[4], was that 87% of patients of all age groups with acute epididymitis requiring hospital admission had positive urine cultures. This does not favour the notion that patients with this condition fall into two groups. Our results confirm that pyrexia, leucocytosis or pyuria do not predict concomitant urinary tract infection in patients suffering from epididymitis. The high rate of sterile pyuria discovered in this study has also been repoted by others[1]. The mechanism by which the infection reaches the epididymis remains unknown. Although reflux of urine along the vas deferens has been postulated[5], it is not known whether the organism which cause urethritis acutally reach the epididymis or whether the urethritis allows the reflux of urine and urethral commensuals[2]. Epididymitis can still occur in men after vasectomy and in these men, the reflux of urine could not have been the machanism. Infection can reach the epididymis through the lymphatics and blood.

A high percentage of patients with epididymitis have sterile urine cultures. Prior antibiotic therapy may increase this proportion. Self treatment with antibiotic is comon in some tropical countries and this complicates treatment. What should be the appropriate treatment for a patient with acute epididymitis whose urine is sterile? Redfern et al 1984[1], suggested that antibiotics be with held from such patients with "idiopathic" acute epididymitis. Chlamydia trachomatis was cultured from 15% of patients in one study and a further 15% had serological conversion. Facilities for culture of chlamydia were not present in our hospital during this study and are available in very few centres in the tropics. If it is accepted that some cases of acute epididymitis in young men result from infection with chlamydia trachomatis, it follows that their female partners need to be treated. There in lies the need to make the facilities for the identification of chlamydia as a cause of infection more widely available.

Although not enountered in this study, acute epididymitis can mimic torsion of the testis[4] or testicular tumour[5]. Though clinical examination is essential in all case of scrotal pain and swelling.

In conclusion, our results do not support the notion that acute epididymitis in young men is of non-bacterial aetiology. We suggest that, at least in the developing countries, antibiotics should be given to all patients with epididymitis. In sexually active patients, in whom chlamydia aetiology is suspected, antibiotic therapy should be extended to their female partners.

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WARFARIN INDUCED SKIN NECROSIS - A RARE CASE REPORT

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Abstract: Skin necrosis is a rare but serious complication of anticoagulation with warfarin. The total number of cases reported worldwide is approximately 200 and only about 73 in the English language literature in the last three decades. Incidence is 0.01% to 0.1% in patients on warfarin therapy. The necrotic lesions appear suddenly, within 3 to 6 days of warfarin administration, are extremely painful, manifest most often in the adipose tissue (buttocks, breasts, thighs) and are most common in middle aged women. They progress from petechiae, ecchymosis, bullae formation finally culminating in gangrenous necrosis. Early recognition of this condition and intervention are necessary to avoid significant morbidity. We present an unusual case of warfarin induced skin necrosis presenting in the fingers and calves of an elderly male with Raynaud's phenomenon.

Key words: Warfarin; Skin Necrosis; Side effects; Anticoagulation.

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Case Report:

A 69 year old male, non-smoker, with history of Raynauds phenomenon was admitted with dizziness, bluish-black discoloration of fingers in both hands and pain with necrotic skin lesions of both calves. Three weeks earlier patient had been hospitalized in a community hospital for evaluation of his Raynauds. Extensive work-up had been done and a diagnosis of 'thrombotic vasculopathy' was made. Patient was started on heparin and subsequently switched to 5 mg warfarin per day, three days prior to the development of the reported presentation. On examination; the patient was stable with blood pressure of 150/80mmHg; no orthostasis; pulse 80/min; temperature 37°C; and respiratory rate 18/min. Examination of the heart, lungs, abdomen and central nervous system were unremarkable; there was bluish-black discoloration of fingers in both hands (fig:1); most severe in the little and ring fingers; the lower extremities revealed multiple, sharply demarcated areas of skin necrosis over both calves with ecchymosis and purpuric spots around the heels (fig:2). The lesions were tender and cool to touch. Distal pulses were felt bilaterally. Laboratory data revealed white blood cell count of 9,400/mm^3; a hemoglobin of 13.4g/dl; and a platelet count of 372,00/mm^3. ESR was 57/hr. The prothrombin time was 30.2 sec (normal 12-15 sec) and the INR (International Normalised Ratio) was 4.8 (normal therapeutic range 2-3). Stool guaic was negative. Chest X-ray, electrocardiogram, echocardiogram and lower extremity doppler studies were negative. Rheumatologic work up and multiple blood cultures to rule out bacterial endocarditis were negative. Serum protein electrophoresis was positive for biclonal gammopathy. Skin biopsy from the necrotic lesions, showed coagulation necrosis with focal heamorrhages, thrombosis of small vessels in the epidermis, dermis and subcutaneous tissue with no active inflammation. After exclusion of other possible causes diagnosis of warfarin induced skin necrosis was made. Warfarin was discontinued. Intravenous heparin, antibiotics, steroids and analgesics were started. Within a few days the necrotic lesions became more oganized. Surgical debridement was done in the calves (fig. 3), followed by full thickness skin grafting and physical therapy. The lesions in the little and ring fingers led to dry gangrene (fig:4) and subsequently to auto amputation. Patient had a prolonged stay in the hospital. Anticoagulation with heparin was continued; warfarin therapy was reinstituted with moderate dosage; after achieving full therapeutic anticoagulation (INR>2.0) heparin was stopped. Patient was referred for rehabilitation and hematology follow up.

Discussion:

Skin necrosis is a rare but serious complication encountered in about 0.01% to 0.1% of patients on warfarin therapy[1,2,3,4]. It is estimated that only 200 cases have been reported worldwide and 73 cases reported in English language literature in the past three decades[2,3,4].

The first symptom of skin injury appears 1 to 10 days after the initiation of warfarin[1] and the peak incidence is between 3 and 6 days in 90% of cases[2,5], however, lesions occurring as late as 16 days[4] and 46 days[5] have been reported. 82% of the patients are obese, middle aged women who are under therapy for thrombophlebitis or

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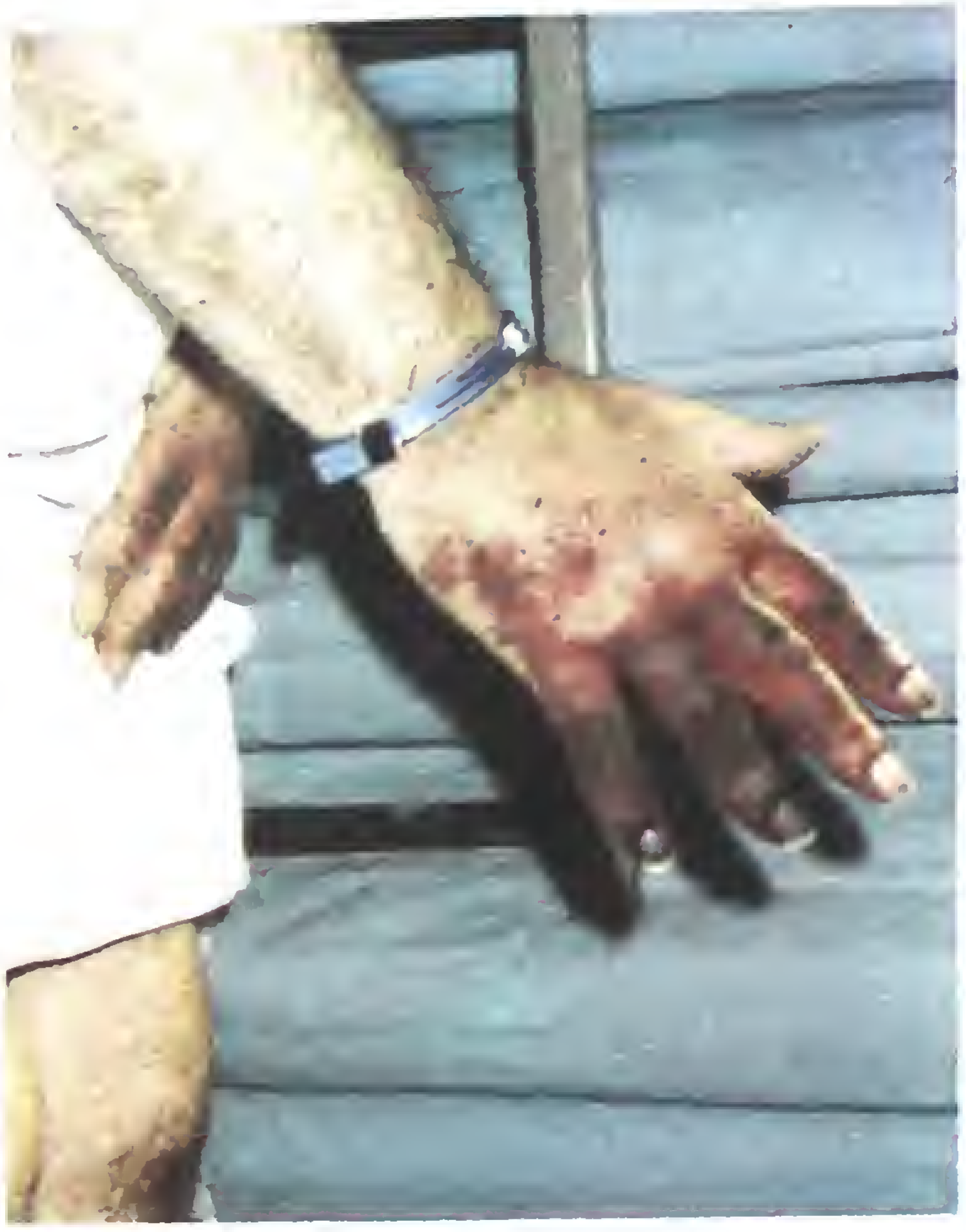

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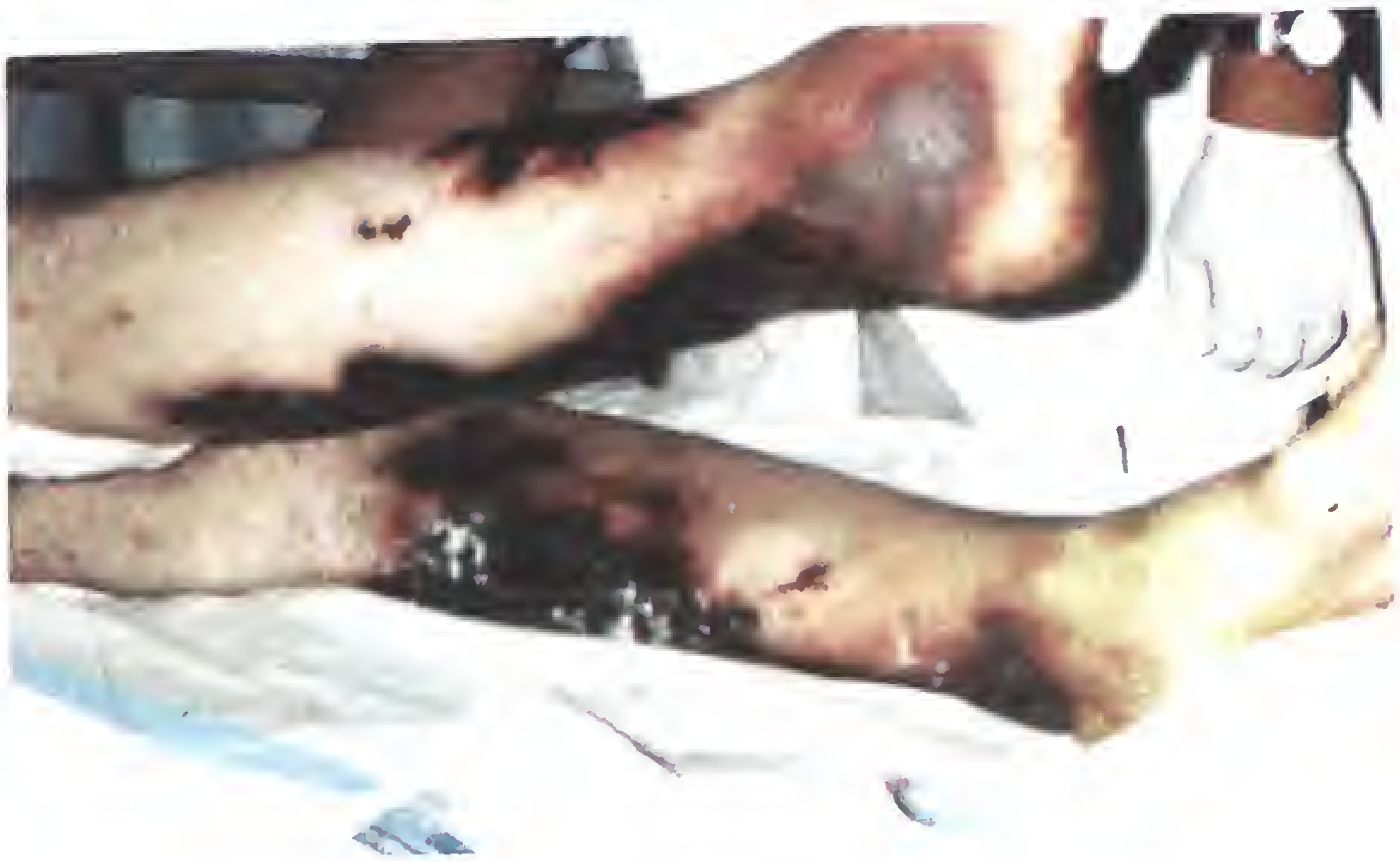

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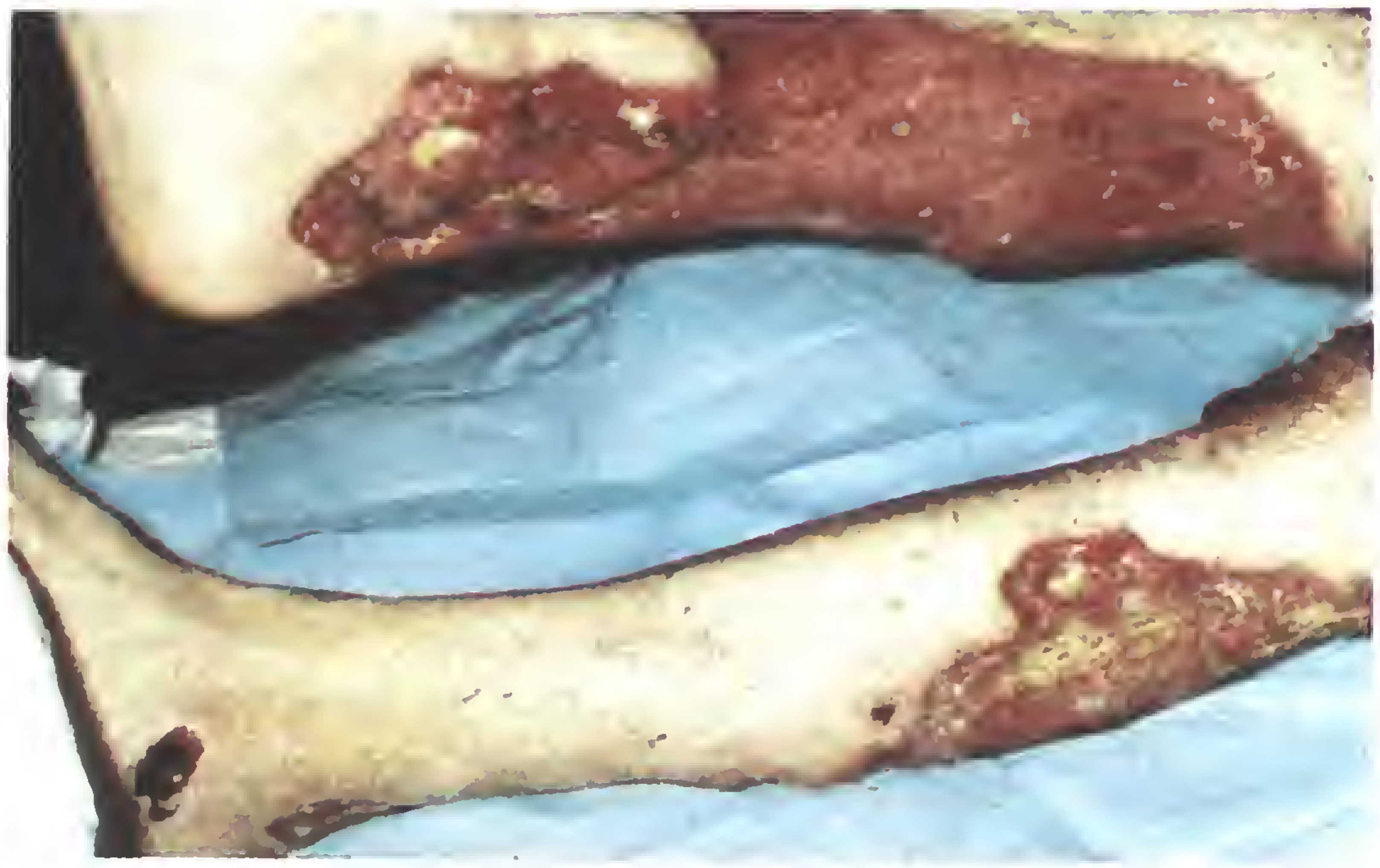

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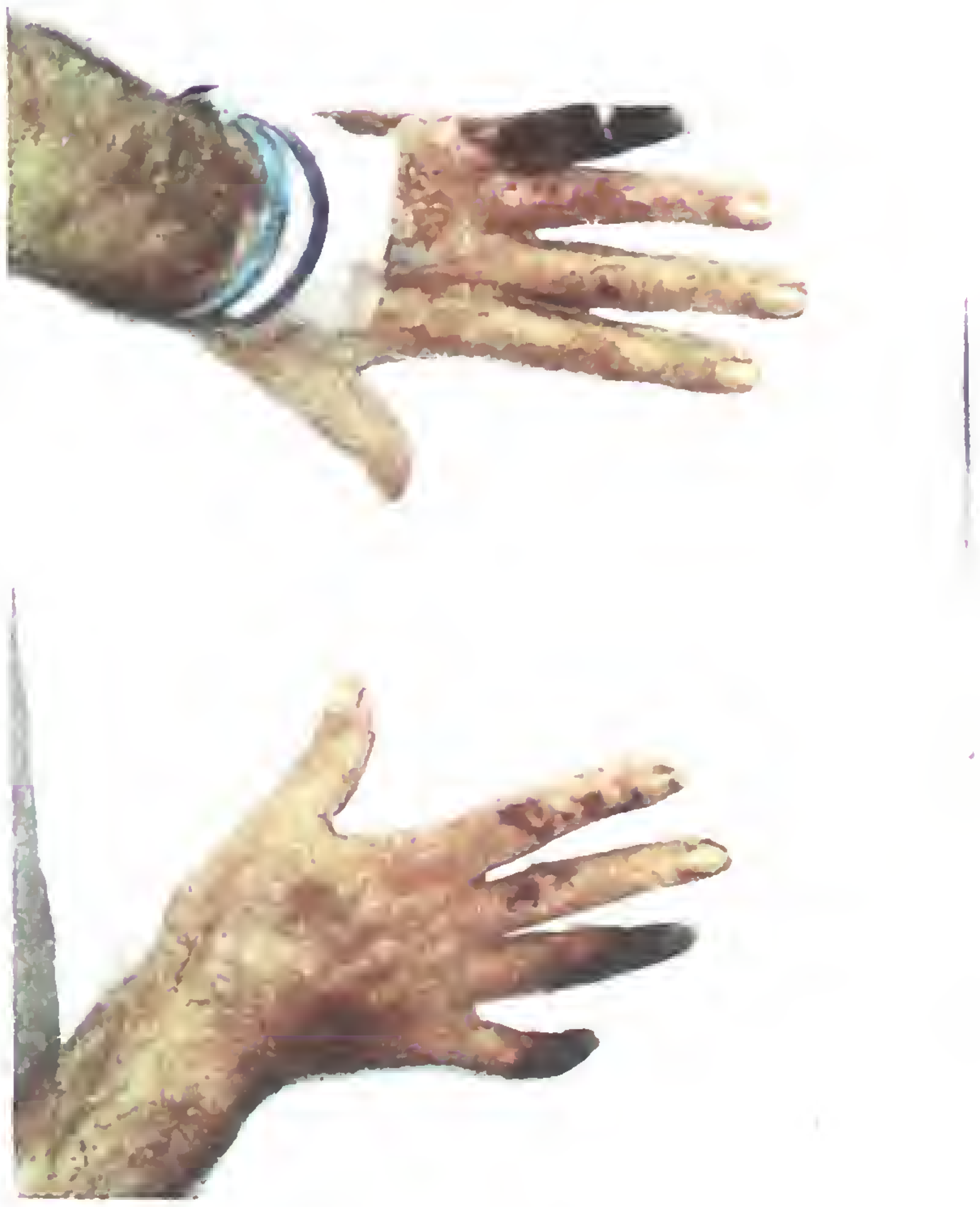

Fig - 4

pulmonary thromboembolism[2,3]. Although 47% to 51% of hospital patients with DVT and pulmonary embolism are men, indicating that both men and women are at equal risk, yet women are 4 times more likely to suffer the complication of skin necrosis. No satisfactory explanation is available for this sex predilection[1]. Typical areas of skin involvement are the areas rich in subutaneous tissue mainly breasts, thighs and buttocks[1,2,3,4,5,6,7]. However, lesions on the extremities, face, male genitalia, abdomen and back have been reported[1,2,3,4].

Although the lesion typically involves one area, 35% of patiennts are affected in multiple sites[3]. The clinical, presentation is both distinctive and predictable. Onset is heralded by pain or evanescent flush followed by petechial hemorrhages which soon coalesce into raddish blue or blue black ecchymosis with a sharply demarcated border and erythematous ring. Within hours to days ecchymosis develops into hemorrhagic bullae which signifies irreversible injury and subsequent full thickness skin necrosis. The necrotic skin lesions soon extend into the subcutaneous tissue. The hallmark is that the muscle is always spared[1,2]. Histologically, the lesions consist of cutaneous infracts extending into the subcutaneous tissue. Extensive thrombosis of dermal capillaries, veins and venules in seen with minimal inflammatory cell infilterate[1].

The pathophysiology associated with warfarin induced skin necrosis is not entirely understood. The creation of a hypercoagulable state, hypersensitivity and direct toxicity have all been proposed as mechanisms for the development of skin necrosis[1,3]. Most reports agree that an early hypercoagulable state which may be associated with warfarin is at least in part responsible. The anticoagulant effects of warfarin occur as a result of disruption in the cyclic interconversion of vitamin K. specifically by inhibition of enzymes vitamin K reductase and vitamin K epoxide reductase, therapy decreasing levels of reduced vitamin K which is required for theactivity of factors II, VI, IX and X. Protein C, a major inhibitor of the procoagulant system and Protein S, which is a cofactor for Protein C are also vitamin K dependent. They inactivate factors V and VII: C, cofactors responsible for the activation of thrombin and factor Xa. Because the half-lives of factor II and protein C are similar (6-7 hours) and considerably shorter than those for factors II, IX and X, the potential for procoagulant activity exists in the first 24-28 hrs of warfarin therapy. A prominent theory suggests that a high loading dose of warfarin may rapidly deplete vitamin K dependent anticoagulants and tigger intravascular thrombosis and skin necrosis independent of prothrombin time. For the same reasons patients with congenital or acquired deficiency of protein C have an increased risk of developing skin necrosis with warfarin[2].

Skin lesions remain localized. Therapy is primarily supportive. Consensus recommendation is to stop warfarin, give parental vitamin K and begin heparin if continued anticoagulation is needed[1]. 50% or more patients require surgical debriment[3] and rarely amputation[2]. Occasionally, severe involvement of a breast or penis have resulted in amputation[6].

Warfarin can be reinstituted when long term anticoagulation is absolutely essential[6]. A loading dose should not be used. Anticoagulation should be started with intravenous heparin, this should be followed with a small to moderate dose of warfarin. After achieving full therapeutic anticoagulation (INR>2.0) heparin should be stopped[6]. Alternativety, successful anticoagulation with LMW heparin for chronic anticoagulation has been tried with very promising results[5].

Our patient, an elderly male with underlying "thrombotic vasulopathy" developed necrotic skin lesions of his fingers and calves on day 3 of warfarin therapy. Significant morbidity was prevented by timely surgical debriment (fig.3). Lesions in the fingers remained confined to the distal digits of little and ring fingers (fig.4) which subsequently led to dry gangrene and auto amputation. Therapeutic anticoagulation was achieved with heparin and warfarin was reinstituted successfully.

In conclusion, this brief case report highlights: a) that warfarin which is a widely used drug in the United States can rarely result in skin necrosis, a very unusual condition with very significant morbidity and even mortality; b) the striking clinical presentation in association with warfarin therapy should allow early diagnosis; however, diagnosis is by exclusion hence other possible causes should be ruled out; c) early recognition and immediate intervention are essential to avoid significant morbidity, and d) Warfarin can be reinstituted successfully in patients in absolute need for chronic anticoagulation.

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VITELLOINTESTINAL DUCT - AN ESCAPING TUNNEL FOR ROUND WORMS

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Abstract: Wandering ascaride may reach many normal or abnormal sites and can cause, acute complications. The patent vitellointestinal duct (VID) is an uncommon anomaly of children which usually presents with faecal discharge from the umbilicus. Rarely, the worm may emerge through it. Two such cases are presented here. These cases emphasize that the children with VID should be regularly dewormed and operated earlier in worm endemic areas to decrease the morbidity.

Key words: Ascaris lumbricoides, Vitellointestinal duct (VID).

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Introduction

Surgical ascariasis, though uncommon in west, is still a formidable problem in certain countries like India. In Kashmir, mostly the children of rural areas, belonging to low socio-economic group with poor hygiene are affected[1]. The adult worm of Ascaris lumbricoides lives in the small intestine, but sometimes may migrate to abnormal sites and cause severe complications, like, intestinal obstruction, small bowel volvulus[2], intussusception[2,3], intestinal perforation with peritonitis[4], acute appendicitis[5], acute pancreatitis, pseudocyst pancreas, acute cholecystitis[6,7] and liver abscess[8,9]. However, worm passing through the patent VID is very rare.

Case No. 1

A 1½ year old male child was admitted in the pediatric Surgery Department of Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, India in August 1998 with the chief complaint of pain abdomen, fever and vomiting of worms, of one week duration. There was history of intermittent umbilical discharge from last one month. There was also history of passage of a round worm from the umbilicus. Clinical examination revealed, a pulse rate of 120/mt, respiratory rate of 30/mt and temperature of 38.2°C. On abdominal examination, there was a serous discharge from the umbilicus (Fig.1), tenderness around the umbilical area and a worm mass in the right lower quadrant. Investigations revealed Hb of 9gm%, TLC of 12,800/Cmm with 82% polys and a normal serum chemistry. Abdominal radiography showed three air fluid levels. The patient was put on conservative management and an ultrasonography was performed which revealed multiple worm masses in the gut even on the second day of admission. The patient was operated with the provisional diagnosis of subacute intestinal obstruction within 36 hours. On exploration, there was a patent VID communicating the distal ileum to the umbilicus and the ileocaecal region was full of worms. Excision of patent VID along with umbilectomy was performed. Worms were removed through the enetrotomy resulting from excision of the VID. Patient was discharged (after deworming) on 7th post-operative day.

Case No. 2

A 2 year old male child was admitted in our department with the history of intermittent abdominal pain, constipation and passage of worms per rectum a month later. There was no history of discharge from the umbilicus. The clinical examination revealed a well nourished child, with inflammatory swelling around the umbilicus without any discharge. Routine blood tests, serum chemistry, and chest radiograph were within normal limits. The abdominal radiographs and ultrasonography showed worm masses in the small gut. On second day of admission while we were evaluating this case of abdominal pain, a worm began to come out of the umbilicus (Fig. II) and was extracterd out with the help of forceps, leaving behind an umblicial fistula. A provisional diagnosis of ascariasis with patent VID was made. Patient was put on antibiotics for 5 days till

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the inflammation subsided. The patient was then explored on 7th day of admission via a transverse subumbilical incision and a patent VID was confirmed. There was a definite communication between the VID and the gut, but to our surprise neither there was any history of discharge from the umbilicus nor it was revealed on abdominal examination. The wedge resection of VID was performed and worms were removed. The patient was discharged on 5th post-operative day and dewormed a week later.

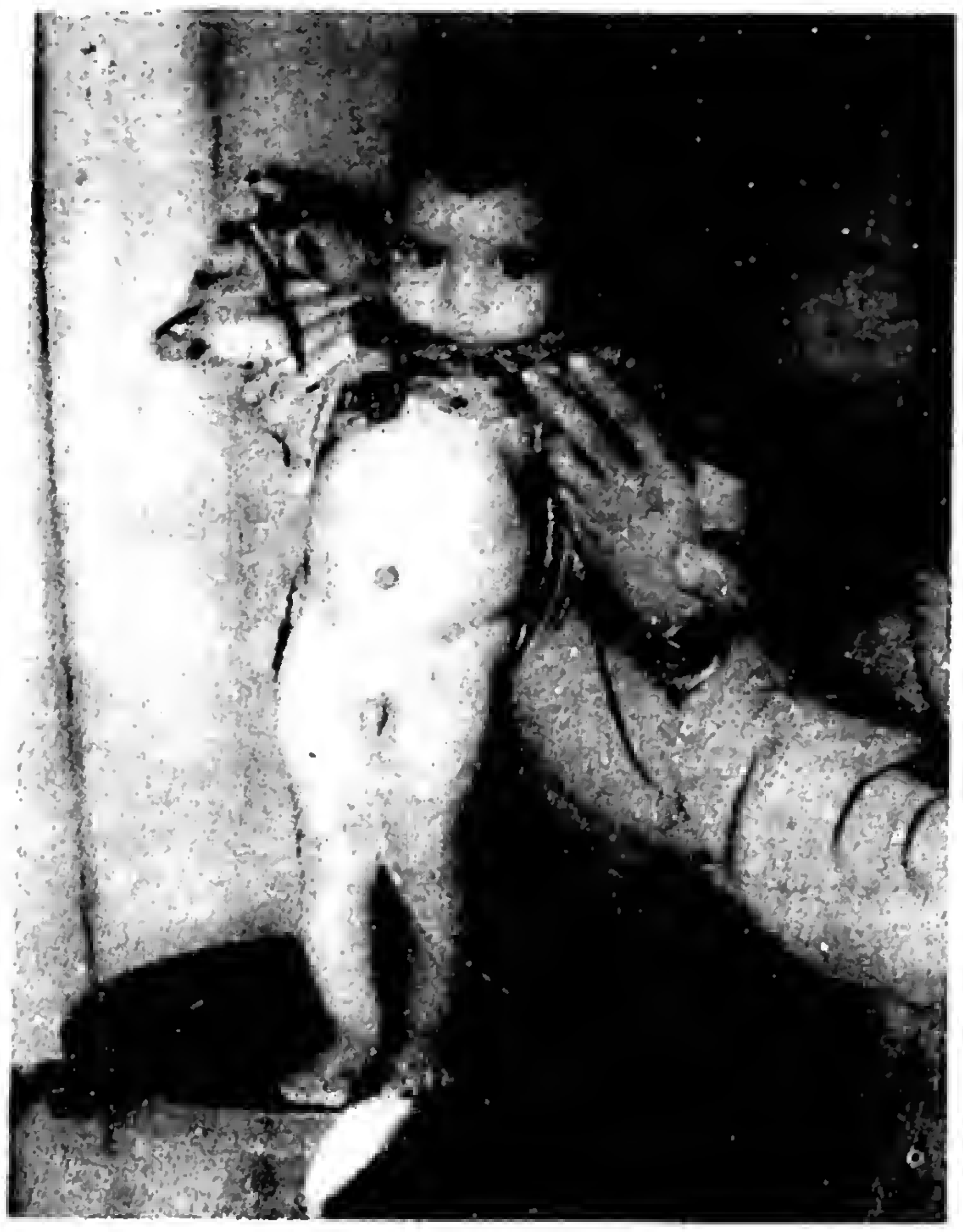

Fig. I: Patent vitellointestinal duct

Discussion

Round worm infestation is very common in India children. There are reports of round worms been recovered from various unusual sites like common bile duct, appendix, eustachian tube,paranasal sinus, pancreative duct, liver abscess and even from heart chamber, but association between patent VID and ascariasis is unique and has been hardly reported in the literature. This may be sometimes the cause of chronic umbilical sinus and omphalitis as happened to be in one of our cases. There are reports that a worm may migrate through a non-communicating VID where there was no through and through communication, possibly worm migrated through the VID, pierced the wall of subumbilical cyst and emerged through the umbilicus. This may be cause for our second case we presented without an umbilical discharge; but on exploration there was a definite communication. This probably may be due to the fact that worms might had already passed unnoticed through the umbilicus giving rise to fibrosed mature track. An ascaride which has not completely come out of an umbilical site should be wrung around the forceps and removed out[10]. The patent VID should be treated on its own merits but when associated with intestinal obstruction an exploratory laparatomy is must to remove the obstructing mass of worms. These cases conclude that if VID is diagnosed it should be operated earlier in worm endemic areas and children be routinely dewormed in order to prevent the complications. These also show that the worm is truly "ubiquitous".

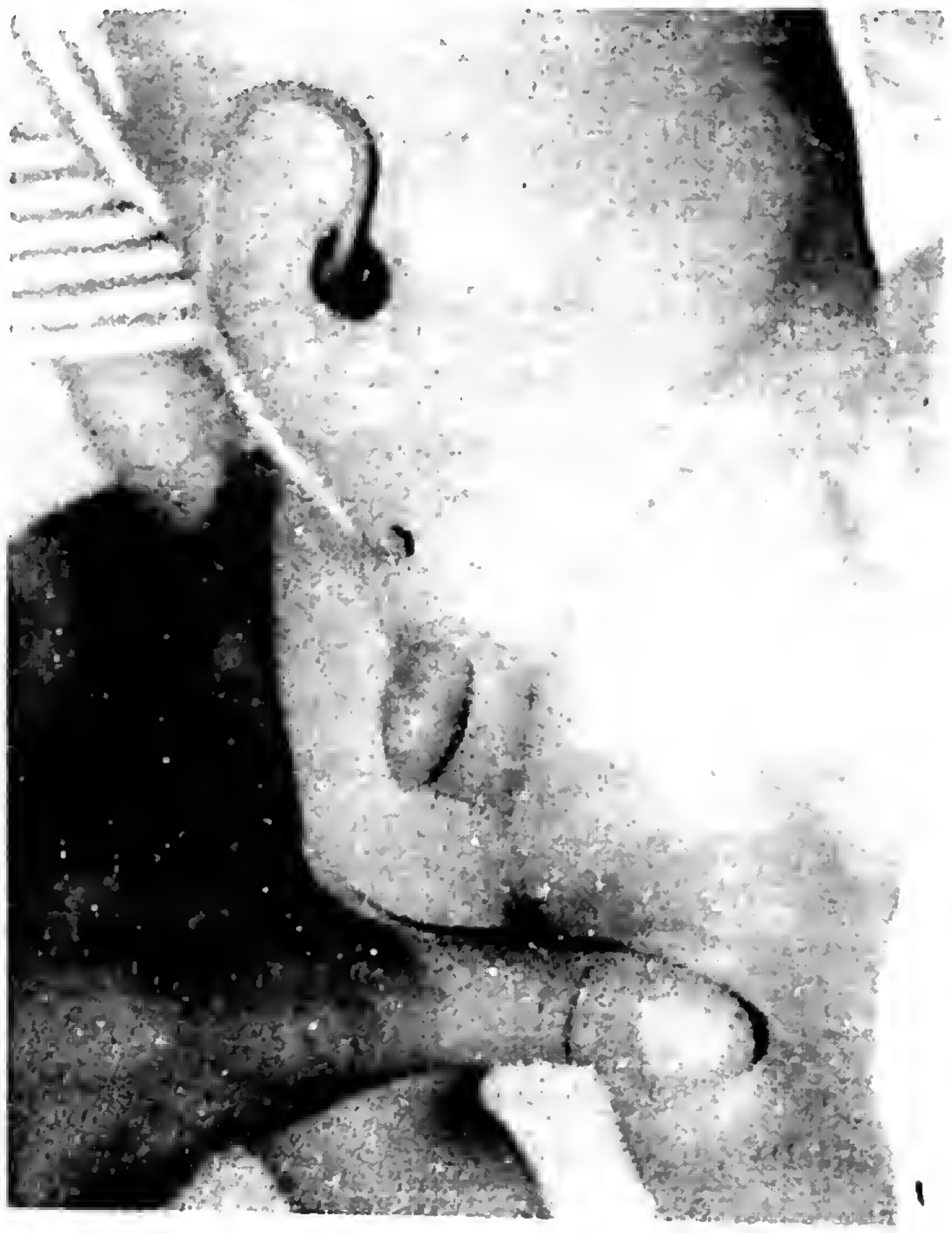

Fig. II: Worm coming out of patent vitellointestinal

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NONHODGKIN'S LYMPHOMA RELAPSING AS INTRAMEDULLARY SPINAL CORD METASTASIS

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Abstract: Intramedullary spinal cord metastasis is a rare complication of malignancies of non-neurogenic origin. A lady with non-Hodgkin's lympnoma who relapsed with intramedullary spinal cord metastasis is described. She received radiotherapy with minimal improvement of the neurologic function.

Key Words: Intramedullary, NHL

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Introduction

Intramedullary spinal cord metastasis (IMSM) is an uncommon complication of malignancies arising outside the central nervous system[1-5]. They have been found to occur in 0.9-2.1% of patients with disseminated malignancy[2,3]. The most common primary tumours that produce IMSM are carcinoma of lung, breast and non Hodgkin's lymphma. In one study, it represented 3.4% of metastases to the spine[1]. IMSM occuring as the first sign of recurrence is rare. We describe a 39 year old lady with non Hodgkin's lymphoma, who relapsed with intramedullary spinal cord deposits.

Case Report:

A 39 year old lady presented with 2 months history of swelling on the right side of neck and fever, followed by cough and hoarseness of voice since one week. On physical examination, she had cervical, axillary and right supraclavicular lymphnode enlargement and features of superior vena caval obstruction. Rest of the physical examination was normal. Haemoglobin was 10.6 gm%, total leucocyte count was 17,100/mm³ and platelet count was 1,78000/mm³. Mediastinal widening was present on the chest X-ray. Lymph node biopsy was diagnostic of non Hodgkin's lymphoma, diffuse mixed cell type. An ultrasonogram of the abdomen, bone marrow biopsy and cerebrospinal fluid (CSF) were normal. She received chemotherapy with cyclophosphamide, vincristine, doxorubicin and prednisolone for 6 cycles at the end of which she was in complete remission. Four months later she presented with weakness of both legs and retention of urine. Neurology examination showed flaccid weakness of all four limbs with grade 4 power in the upper limbs and grade 2 in the lower limbs along with a right sided facial weakness of lower motor neurone type. Tendon jerks were exaggerated. Respiration was compromised. There was sensory impairment below C_5 level. Her higher mental function were normal and cerebellar signs were absent. CSF examination showed a protein level of 44 mg/dl, sugar of 30 mg/dl, and few lymphocytes. Magnetic resonance imaging of the brain and spinal cord done showed multiple intramedullary deposits at C_1 and C_4 level with cord swelling, and a brain parenchymal lesion in the right hippocamppal region (Figs. 1&2). She received radiotherapy to the cervical spine (40 Gy) steroids and physiotherapy. There was only minimal improvement in the neurologic function. The disease progressed and the patient died.

Discussion:

Intramedullary spinal cord metastasis arising from primary tumors outside the CNS are believed to be rare, often found only at autoopsy[2,3,6,7], and the diagnosis of IMSM metastatsis may be elusive in the clinical setting. Among the non neurogenic malignancies which throw IMSM, the most common primaries are lung, breast and non Hodgkin's lymphoma, followed by melanoma, colorectum, kidney, head and neck tumors and Hodgkin's lymphoma[1,2,5,6]. IMSM develop from haematogenous dissemination or by leptomeningeal spread with secondary invasion of the spinal cord[5,6]. The thoracic cord is the most common site of IMSM of non neurogenic origin followed by the cervical cord[6].

Patients with IMSM often present with symptoms of short duration. Pain and weakness accompanied by bowel and bladder dysfunction and sensory loss are the

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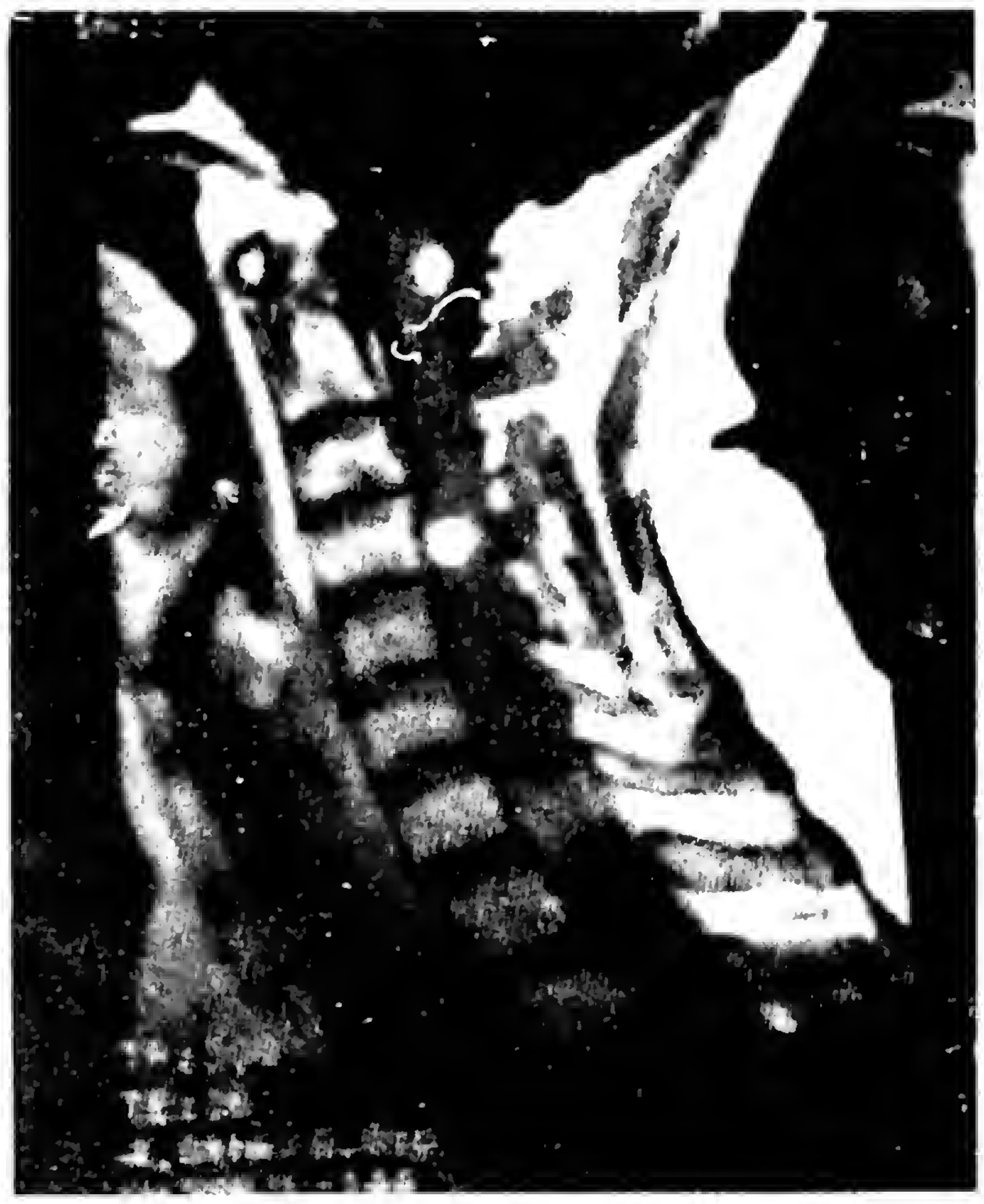

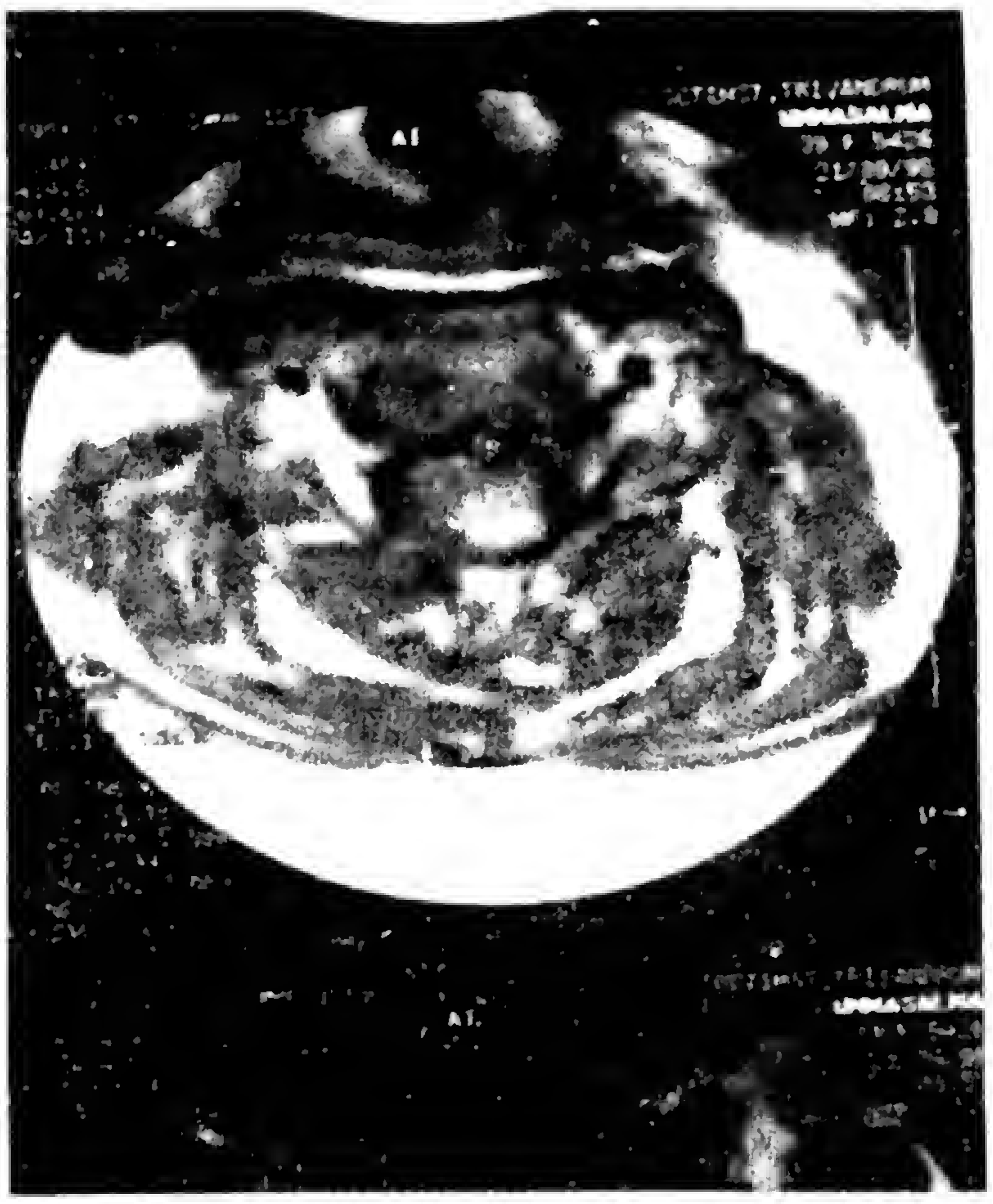

Fig - I *NHL Relapsing as intramedullary spinal cord metastasis* *Fig - II*

most common presenting complaint[1,4,6,7]. Rarely, a patient presents with an IMSM as the the first manifestation of malignancy[8]. Neither the clinical picture nor CSF examination findings help in differentiating IMSM from epidural metastasis, leptomeningeal carcinomatosis, paraneoplastic and radiation myelopathy or other causes of myelopathy. Myelography also fail to show early IMSM. Magnetic resonance imaging (MRI) is the diagnostic modality of choice here, as in other intramedullary spinal cord lesions. MRI usually shows expansion of the spinal cord in T1 weighted images and focal areas of contrast enhancement. On T2 weighted images, there is usually high signal intensity and cord expansion. Contrast with Gadolinium DTPA differentiates the tumor from oedema and fibrosis. Associated leptomeningeal metastasis may also be evident[8]. Other conditions which produce contrast enhancing intramedullary lesions include primary spinal cord tumors, transverse myelitis, sarcoidosis, radiation myelopathy[8]. In our patient also, the diagnosis was clinched by MRI.

Prognosis of these patients appears to be grim, despite radiation therapy. Survival is very short, with 80% dying within 3 months[6] due to rapid neurologic deterioration and to the progressive systemic cancer[2,4,6,7]

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SOFT TISSUE AND BONE HEALING IN A COMPOUND FRACTURE TIBIA WITH A NEGLECTED EXPOSED DYNAMIC COMPRESSION PLATE: A CASE OF NATURAL HEALING

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***Abstract:** A case of compound fracture tibia was operated about 7 years back and stabilised with dynamic compression plate. Subsequent desloughing for necrosis of the overlying skin exposed the whole of plate and most of tibia. Secondary infection was managed with wound care and antibiotics. The nature offered its own cure by epithelisation over the invading soft tissues which even covered the bone under the plate. The whole plate remained exposed throughout these seven years which is probably the longest time a plate has been kept exposed over the bone.*

Key words: Compound Fracture Tibia - Plating - Wound Coverage

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Introduction

If a compound fracture of a bone after stabilisation by an internal fixation device like a plate gets exposed due to sloughing of overlying soft tissue, a viable soft tissue coverage from another site, is often needed for proper wound healing. The soft tissue coverage may be achieved by different procedures like relaxing skin incisions, muscle transposition, cross leg flaps, myoplasty etc. depending upon the area of loss or it may grow from the surrounding soft tissues and may gradually even cover the plate. We report a case in which soft tissue coverage as well as overlying epithelisation had occured even under the plate when plate had been kept exposed for seven long years.

Case Report

A 45 year old man was injured 7 years back in a vehicular accident resulting in type II compound fracture of right tibia. He was operated within four hours of injury. Wound debridement was done and dynamic compressioin plate applied over the tibia. Within few days whole of the plate along with most of the bone got exposed due to sloughing of the overlying skin on medial side and patient developed wound infection. The patient was put on cephalexin and gentamycin after culture and sensitivity report for three weeks. While waiting for the wound infection to get controlled for the subsequent soft tissue covering procedure, the granulatlion tissue continued to grow from the surrounding tissues leaving only the plate exposed. The patient was lost to follow up when he returned back after a gap of 7 years with fully exposed plate over medial aspect of the leg (Fig.1). He had been involved in manual labour throughout this period and did not bother to remove this exposed plate for fear of breaking the bone.

Roentgenogram showed fracture united with good amount of callous (Fig 2). After convincing the patient about fracture union the plate was removed without anaesthesia. Removal of plate exposed a dark brown crust underneath (Fig 3). Removal of this crust exposed shiny skin covering the bone (Fig. 4).

Discussion:

Failure of wound healing from skin necrosis, breakdown and secondary infection frequently results from attempts to close a wound or incision under significant tension. In case of extensive loss of soft tissue, it is desirable to cover exposed bone but it is not always necessary to cover it with skin. Different procedures have been utilised to cover exposed bone or plate. Muscle bellies may be shifted locally, relaxing incisions in the skin occasionally may be used to shift normal skin and subcutaneous tissue over the bone, but great care and planning are necessary to do this successfully. Extensive myoplastic or cross leg flaps are reserved for closure of large defects as secondary procedure[2,5].

Different authors advocate keeping the infected implant in situ in case of early infection till fracture stability and granulation tissue covers the bone[1,4].

The present case is unique in the sense that it is probably the longest time in literature that a plate has been kept exposed. No cross leg or myoplastic procedure

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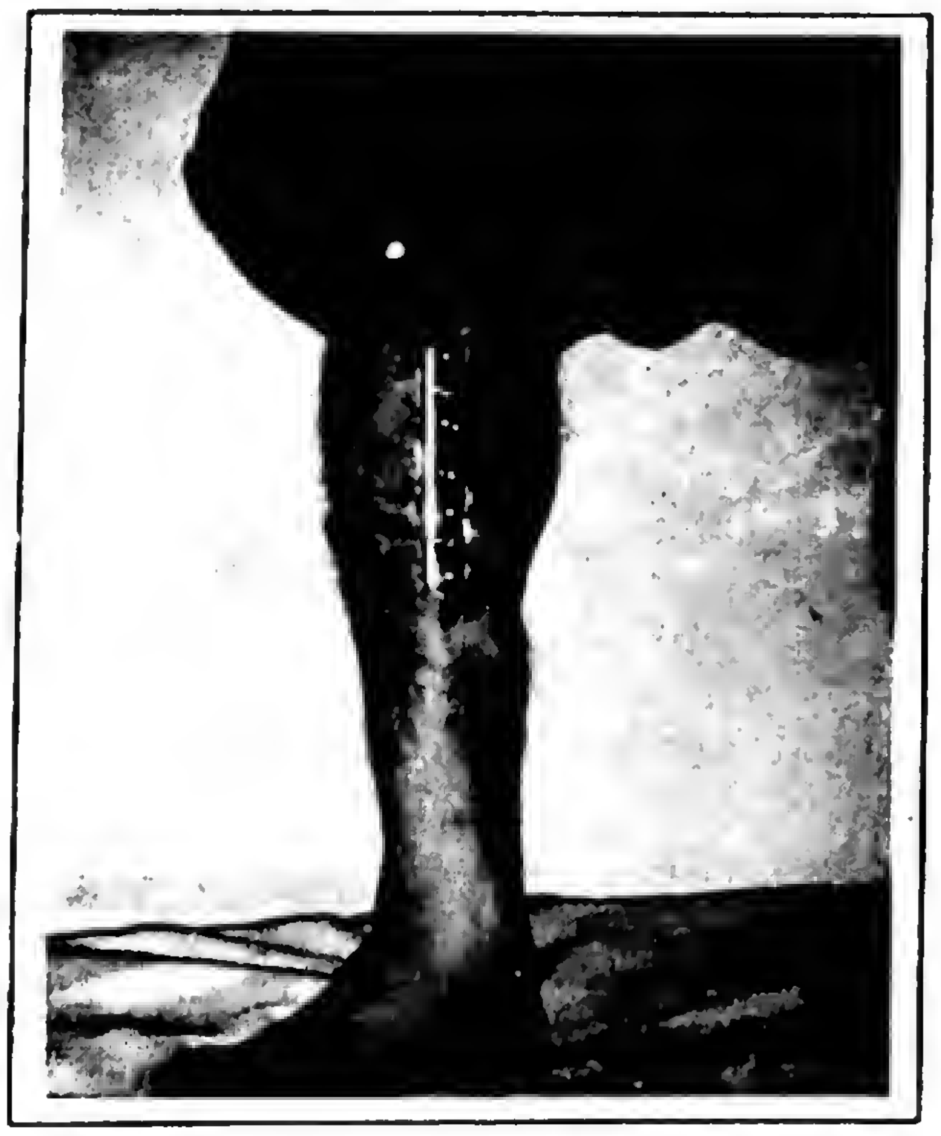

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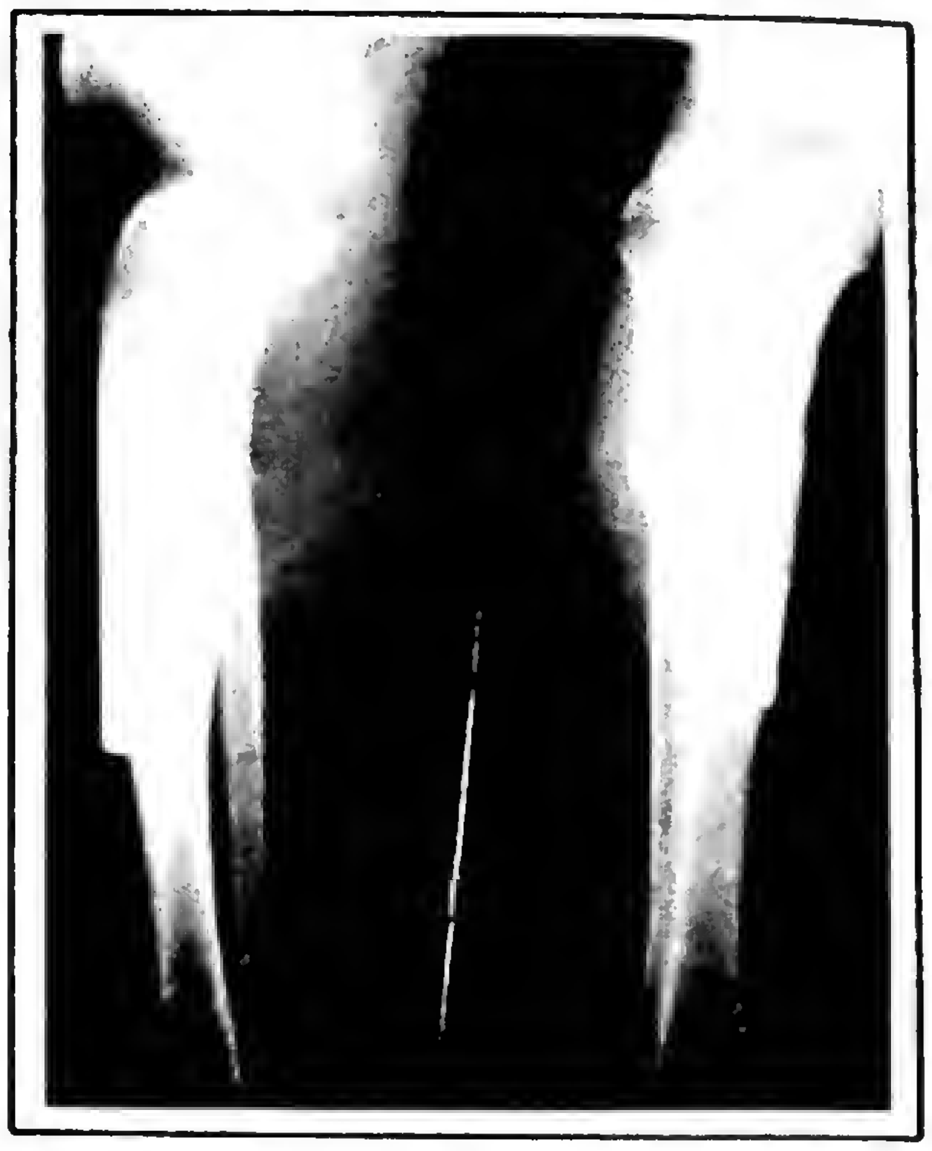

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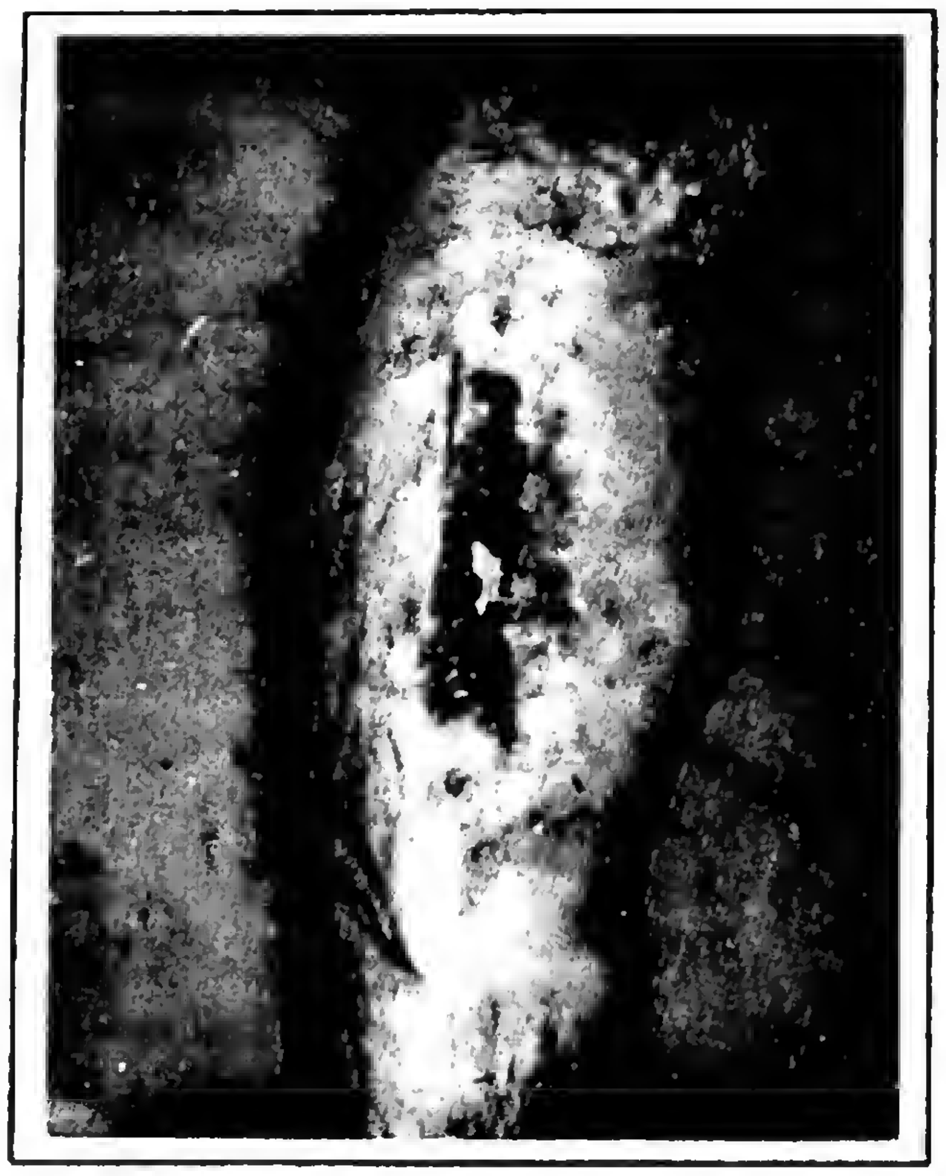

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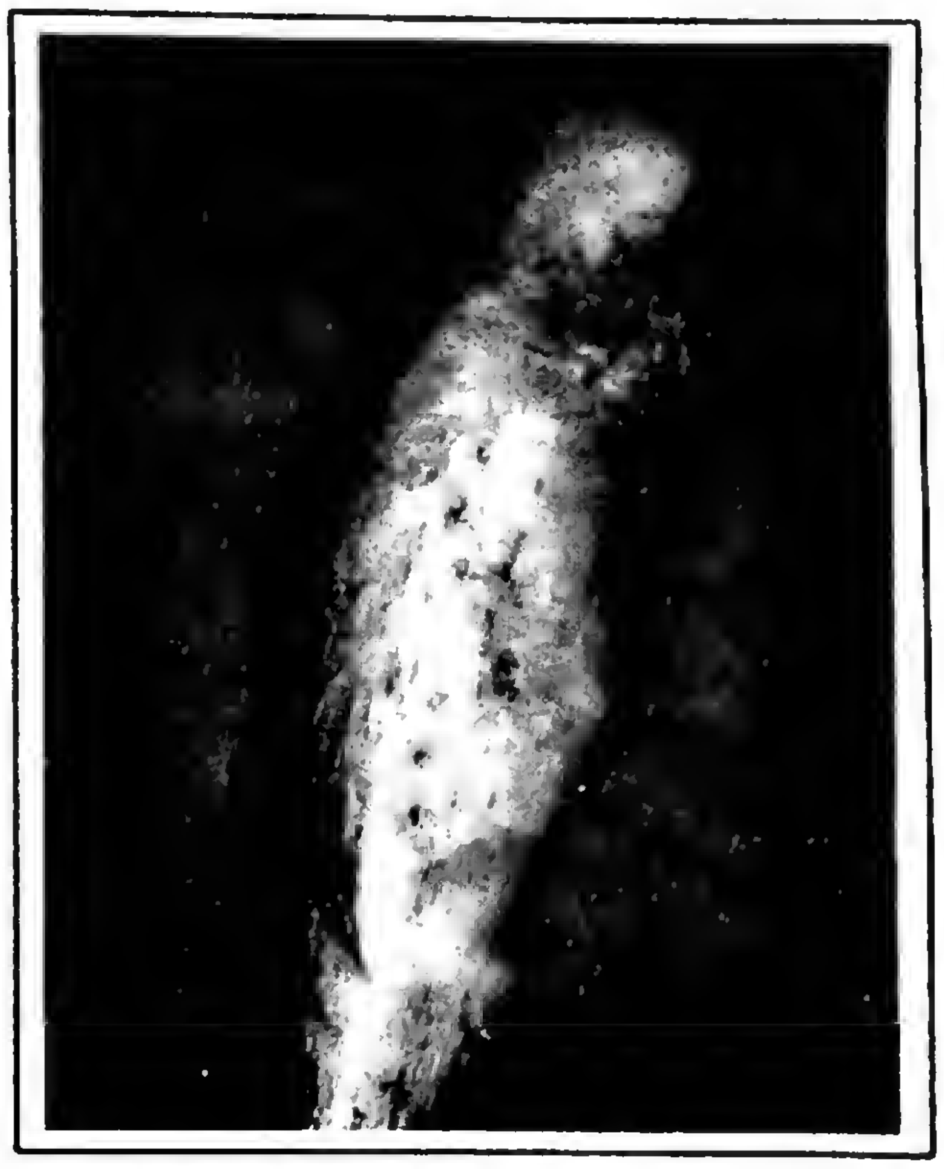

Fig - 4

was done to cover the exposed plate. In the course of time granulation tissue covered the bone and there was epithelisation under the plate while as bone healing took its own course. The epithelisation of tissue under the plate resulted probably either from invasion of surrounding tissues because of loosening of plate in due course of time or metaplasia of underlying tissues. The disadvantage being the longer time taken for the soft tissue coverage which could have been hastened by covering procedures.

Time is a great healer and nature takes its own course. One should not be horrified by an exposed plate bridging a fracture, it will still serve its purpose of fracture stability and providing environment for soft tissue healing by splinting the bone.

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URETERIC INJURIES AT TOTAL ABDOMINAL HYSTERECTOMY-CASE REPORTS

Wani M.Saleem M.S; P.B.Singh M.S; U.S. Dwivedi M.S.

Abstract: The intimate proximity of female genital organs to the ureter make the latter more susceptible to injury during Gynecologic surgical interventions. We present two cases of ureteric injury following total abdominal hystrectomies.

Key words: Ureteric Injury, Hysterectomy.

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Case Report -1:

A 40 years old women was referred one and half months after total abdominal hystrectomy with persistent vaginal dribbling of urine. The intravenous urogram (IVU) showed bilateral hydroureteronephrosis more severe on left side with non visualization of both distal ureteral ends. At cystoscopy no fistulous tract communicting with bladder was demonstrated. Ureteric catheterasation was attempted but the catheter could not be negotiated beyond three cm on right side and six cm on the left side. At operation the left dilated ureter was seen embeded in the fibrous tissue six cm from the bladder while as, the right one was encased in dense adhesions two to three cm from the uretero vesical junction. A right uretero neocystostomy and left Boari's flap procedure was performed in non-refluxing fashion. The patient made an uneventful recovery and his IVU at three months after surgery showed marked improvement in degree of hydroureteronephrosis.

Case No.2:

A 32 years old women presented with dribbling of urine per vaginum on 7th post operative day following total abdominal hystrectomy done for dysfunctional uterine bleeding. The patient was managed conservatively for 40 days without any improvement and was referred for specialized care. The ultrasound examination revealed mild dilation of left pelvicalyceal system, and IVU demonstrated left hydroureteronephrosis with non delineation of distal segment of the ureter.

Ureteric block at six cm was demonstrated on ureteric cathete, risation. At operation left ureter was obscured by dense fibrous adhesions. The ureter was divided proximal to the block and anastamosed to boari's flap. The patient made an uneventful recovery.

Discussion:

The ureteral obstruction can occur not only secondary to ligation of ureter but also can be due to its crushing, kinking. leceration, devitalization and transection[1]. The incidence of ureteric injury during routine hystrectomy varies from 0.5 to 3 per cent, and when it occurs it is bilateral in approximately one of every six cases[2]. The close proximity of distal ureter to the uterine artery makes it prone to injury if proper care is not taken while applying clamps on the vessel[3].

The most common sites of ureteral injury are:- (1) In the ovarian fossa, (2) In, fundibulo-pelvic ligament, (3) Where the ureter crosses dorsal to uterine artery and; (4) In the vesicovaginal space[4]. These two cases demonstrate morbidity which can result following ureteric injury.

Obviously, the best treatment for intraoperative ureteral injury is prophylaxsis, and the safest policy to prevent morbidity is to detect the injury early and correct it before the upper tract deterioration occurs.

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SLE PRESENTING AS LONG STANDING PSYCHOSIS- A RARITY

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Abstract: *Reported here is probably to our knowledge the longest duration case of psychosis prior to its diagnosis of systemic lupus erythematosus (SLE). Although CNS involvement in SLE is well known, yet long standing psychosis because of disease is a rarity. In the absence of steroid therapy and disfigurement of face because of disease, the neuropsychiatric manifestations may be accounted for by widespread microinfarcts in cerebral cortex.*

Key words: *SLE, Psychosis.*

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Introduction:

SLE is a multisystem disease with continously changing phenomenon[1]. This disease has protean clinical manifestations and varied immunological abnormalities[2]. At onset SLE may involve only one organ system, additional manifestations may occur later on, CNS events may vary from solitary to mumerous presentation. Psychosis is not a less frequent manifestation of SLE[3], we present here a case of SLE who had only psychosis for 5 years and remained undiagnosed and unsuspected till she developed other features of SLE, Her clinical picture including psychosis improved remarkably with steroid therapy.

Case Report:

A 25 year old lady was being treated for psychosis for about five years. There was no apparent metabolic or organic cause for her psychosis. Over a period of past five months, she developed erythematous rash on face, fingers and feet. In addition to rash, she also noticed malaise, decreased appetite, joint pains and loss of hair. There was no history of Raynauds phenomenon, seizures or arthritis. On general physical examination, she was found to be anaemic, with a blood pressure of 150/100mmHg. Cutaneus examination revealed butterfly rash on face, erythema of dorsum of fingers and toes with sparse scalp hair. Except for ascites, systemic examination was unremarkable. Neuropsychiatric evaluation revealed features suggestive of organic psychosis. Investigations revealed haemoglobin of 7.2gm%, TLC 700/mm^3, neutrophils 60%, lymphocytes 35% and eosinophils 5%. Peripheral blood film showed microcytosis with hypochromia. ESR was 60mm in Ist hour (Westergens), coagulogram was normal. Urine analysis showed a proteinuria of 4gm/day, with microscopic haematuria, and a few granular casts. Ascitic fluid was found to be transudative. Serum ANA,anti-ds DNA, anti-Sm antibody and rheumatoid factor were positive. However, serum VDRL, HBSAg, LE cell phenomenon, cryoglobulin and combs test were negative. Similarly, chest skiagram, ECG, thyroid function tests, echocardiography, CSF analysis, EEG and cranial CT scan were unremarkable. Skin biopsy showed thinned out epidermis with basal cell degeneration and spongiosis of upper dermis, Renal biopsy and MRI of brain could not be done. With aforementioned clinical and laboratory features, a diagnosis of SLE was entertained as the patient fulfilled all the requisite 1982, ARA criteria for SLE[4]. Three weeks after receiving prednisolone in a dosage of 1.5mg/kg/day, there was remarkable improvement in her clinical picture. Patient was followed up for 12 months and remained symptom free. After 4 months steroids were gradually tapered without any recurrence of psychosis.

Discussion:

SLE is a disease with continuously changing phenomenon. A large number of cases are either not diagnosed or remain unsuspected for a long time thereby being denied the benefit of therapy. Close and continous watch is absolutely essential[1]. The cummulative frequency of neuropsychiatric manifestations in SLE has been found to vary from 3 to 63%[3-9], but neuropsychiatric features presenting as the initial manifestation of SLE has been found to be 3.7%[10-12]. The patient under discussion had psychosis for about five years with no other features of SLE. Nevertheless, a delay in diagnosis of SLE by a few months is not unusual[2], but long standing

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psychosis preceding other manifestations of SLE have been attributed to microinfarcts in the cerebral cortex[3,14]. Although psychosis is an uncommon feature of SLE, yet the diagnosis of SLE shoud be considered when there is not other clue to the aetiology of psychosis.

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TYPE-I, SECOND DEGREEE AV BLOCK AFTER PERCUTANEOUS LIVER BIOPSY - A RARE COMPLICATION

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Abstract: *Complications associated with percutaneous liver biopsy are infrequent with experienced hands. The most common complication following this procedure are pain and hypotension and are mediated by vagus nerve[1]. Bradyarrhythmias in the form of AV blocks occuring as a result of percutaneous liver biopsy havenot been reported so far. Our patient developed transient and reversible type-I, second degree AV block following percutaneous liver biopsy.*

Key word: *Precutaneous Liver liopsy, Second degree AV Block.*

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Case Report

20 year old boy was admitted in the department of Gastroenterology at Sher-i-Kashmir Institute of Medical Sciences, Srinagar with mild icterus of 1 year duration. Patient had arthralgias and was complaining of weakness and easy fatiguability. Clinical examination revealed icterus, liver 6 cm below right costal margin and spleen 5cm below left costal margin. There was no free fluid in the abdomen. Chest, cardiovascular and neurological examinaltion was normal. Investigations revealed hemoglobin of 15 g/dl with normal complete blood counts and renal parameters. Electrocardiogram on admission was normal. Liver function tests revealed serum bilirubin 5.2 mg/dl, serum aspartate aminotransferase 370 U/L, serum alanine aminotransferase 420 U/L; alkaline phosphatase 340 U/L, total proteins 7.2 g/dl, albumin 3.2 g/dl, globulin 4 g/dl. Hepatitis virus (B and C) seromarkers were negative. Antinuclear antibodies and rheumatoid factor were positive. Immune markers especially L.K.M. could not be studied due to nonavailability of facilities. However, Wilsonian profile was normal. With provisional diagnosis of autoimmune hepatitis, the patient was subjected to percutaneous liver biopsy for diagnosis and ascertaining the HAI (histologic activity indes). Liver biopsy was done and 2cm fragment of liver tissue was obtained and send for histopathological examination. While observing the patient post liver biopsy, patient was detected to have developed irregular pulse without any hemodynamic compromise. Electrocardiogram revealed type-I, second degree AV block. Cardiology opinion was sought and patient was observed in intensive cardiac care unit for 24 hours. Patient continued to be asymptomatic and reverted to sinus rhythm.

Discussion

Liver is a highly vascular organ and has rich sympathetic and parasympathetic innervation[2,3]. A hospitalization rate of 1.4 to 3.2% for the management of a complication following perctaneous liver biopsy has been reported, with pain or hypotension being the predominant cause[1] Acute transient hypotension with abdominal or lower chest pain but without tachycardia immediately after percutaneous liver biopsy has been described. The local baro-receptors capable of detecting sinusoidal pressure have been thought responsible for hepato-renal syndrome[4,5]. Afferent impulses of the same reflex arc, transmitted through vagus, are responsible for pain and various pain mediated vasodepressor manifestation result in various bradyarrhythmias and hypotension[6]. After screening the literature extensively, we could not find any bradyarrhythmia associated with percutaneous liver biopsy. To the best of our knowledge this is the first case report of type-I, second degree AV block associated with percutaneous liver biopsy.

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TRANSITIONAL CELL CARCINOMA OF THE LOWER THIRD OF THE URETER

S. Kumar M.S.; B.K. Jalali M.S.; A. Ganju M.S.

Abstract: Tranistional cell carcinoma of the ureter is an uncommon urothelial malignancy which most commonly present with haematuria & non-functioning kidney. This patient presented to us with less common presentation of flank pain without haematuria. Tumours of lower third of ureter can be successfully managed by segmental ressection and ureteric reimplantation.

Key Words: Urothelial malignancy, ureteric reimplantation, ureteroneocystostomy.

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Introduction

Ureter is the least favoured site for urothelial malignancies with 90% of tumours occuring in bladder, 6-8% in urethre & 2-4% in renal pelvis & ureter[1]. The initial and most common presentation is gross haematuria with a poorly functioning or non-functioning kidney on intra venous pyelogram (IVP).

Case Report

A 50 year old female presented to us with history of dull pain off & on in the left lion for last one year. There was no history of haematuria, fever, analgesic abuse. There was no palpable mass in the lumbar region.

On investigating the patient, Hb was 9.8gm%, TLC-9600/cc, DLC-P61, L35, E02, M02, BO & ESR - 10mm (at end of Ist hour by Westergren's method). Blood urea & serum creatinine were 19mg% and 0.8mg% respectively. Urine on routine microscopy showed 110-12 pus cells per high field. No RBC's were seen. Xray of kidney, ureter and bladder region didn't reveal any radiopaque shadow, Ultrasound scanning of abdomen showed hydronephrosis of left kidney with kidney size of 14 x 12 x 5 cm. Left ureter was not visualised. Right kidney and ureter were normal. IVP revealed a non-functioning left kidney. Right kidney and ureter were normally visualised.

In view of the ultrasound and IVP findings a provisional diagnosis of left hydronephsosis due to pelvic ureteri junction (PUJ) obstruction was made and it was decided to explore the kidney through the bed of the 12th rib. On exploration there was no evidence of PUJ obstruction. On the contrary left kidney and pelvis were enlarged and distended and left ureter was grossly dilated and torturous along its whole length upto the pelvic brim as visible from the flank incision.

From the aforementioned findings it was apparent that the cause of obstruction lay lower down. A second incision was therefore made in the lower abdomen to explore the lower third of the ureter and bladder. The ureteric dilatation was found to extend right upto the bladder wall. Bladder was opened; both the ureteric openings looked normal. A curved haemostat was gently introduced into the normal looking left ureteric opening. On withdrawing the haemostat a small frond like growth pouted out. A little tug with a non-toothed forceps brought out more of the papillomatous growth into view. It was now clear that gross dilatation of the kidney, pelvis and ureter was due to this growth which was tightly filling the intramural juxtavesical part of the ureter. Segmental ressection of ureter & culf cystectomy was done. Laying open the excised segment of the ureter

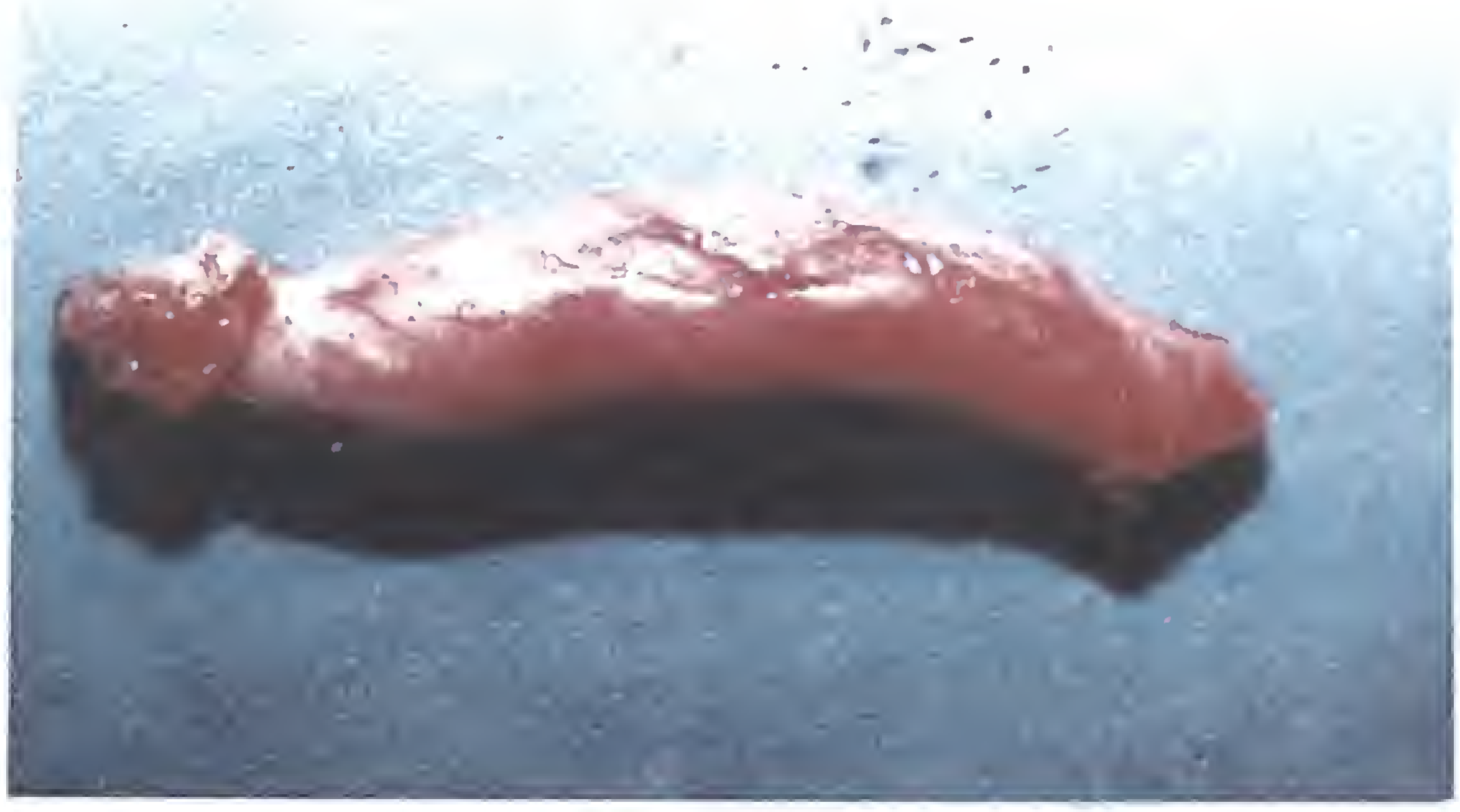

Fig.I: Showing growth bearing ureter with cuff of bladder

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revealed a large pendunculated growth which was tightly packed inside the lumen of the ureter and a smaller rather sessile looking mass about 2cm further down. Histopathology showed a moderately differentiated transitional cell carcinoma with resected margins free of the growth.

Discussion

Ureteral tumours are rather uncommon with one fourth the incidence of renal pelvis tumours[2] with 73% occuring in lower third of ureter, 24% in mid-ureter & 3% in upper third of the urter[3].

Unlike in our patient,haematuria is the most common presenting symptom, seen in 60-75% of cases[4]. Flank pain, with which this patient presented to us is a dull ache and non-radiating and occurs only in 30% of ureteral tumours.[5] In view of the IVP & ultrasound findings a diagnosis of PUJ obstruction (probably the commonest cause of silent hydronephosis) was made and decided to explore the kidney on affected side.

The type & extent of surgery advocated for ureteral tumours depends upon the location and grade of the tumour. Upper & mid ureteric tumours should be treated with segmental ressection if these are solitary and low grade and nephroureterectomy if these are multifocal and high grade[5].

The chances of ipsilateral recurrence are as high as 50% if segmental ressection is attempted in high grade tumours.[6,7]

The tumours in the third of ureter whether high grade or low grade are successfully managed by segmental ressection with cuff cystectomy with ureteroneocystostomy as chances of recurrence in the proximal segment are rather remote[3]. No significant difference in 5-year survival of patients was seen with lower third ureteral cancers treated by either nephroureterectomy (5 year suvival 47%) or segment ressection (5 year survival 55%).[8]

Contralateral recurrence occurs in less than 2% of patients[9] but 30-75% of patients develop bladder tumour at some point of time[2]. This suggest a need for routine follow-up cystoscopy in patients with upper tract tumours.

It is difficult to draw a definitive conclusion regarding the ureteroscopic approach and role of radio therapy and local and systemic chemotherapy in the management of these tumours as the data available in literature is very limited.

Conclusion

Lower third ureter cancers are rare urothelial malignancies which most commonly present with haematuria and non-visualisation of kidney on IVP but may present with flank pain only. These can be successfully managed by segmental ressection with cuff cystectomy and ureteric reimplanatation rather than attempting nephoureterectomy.

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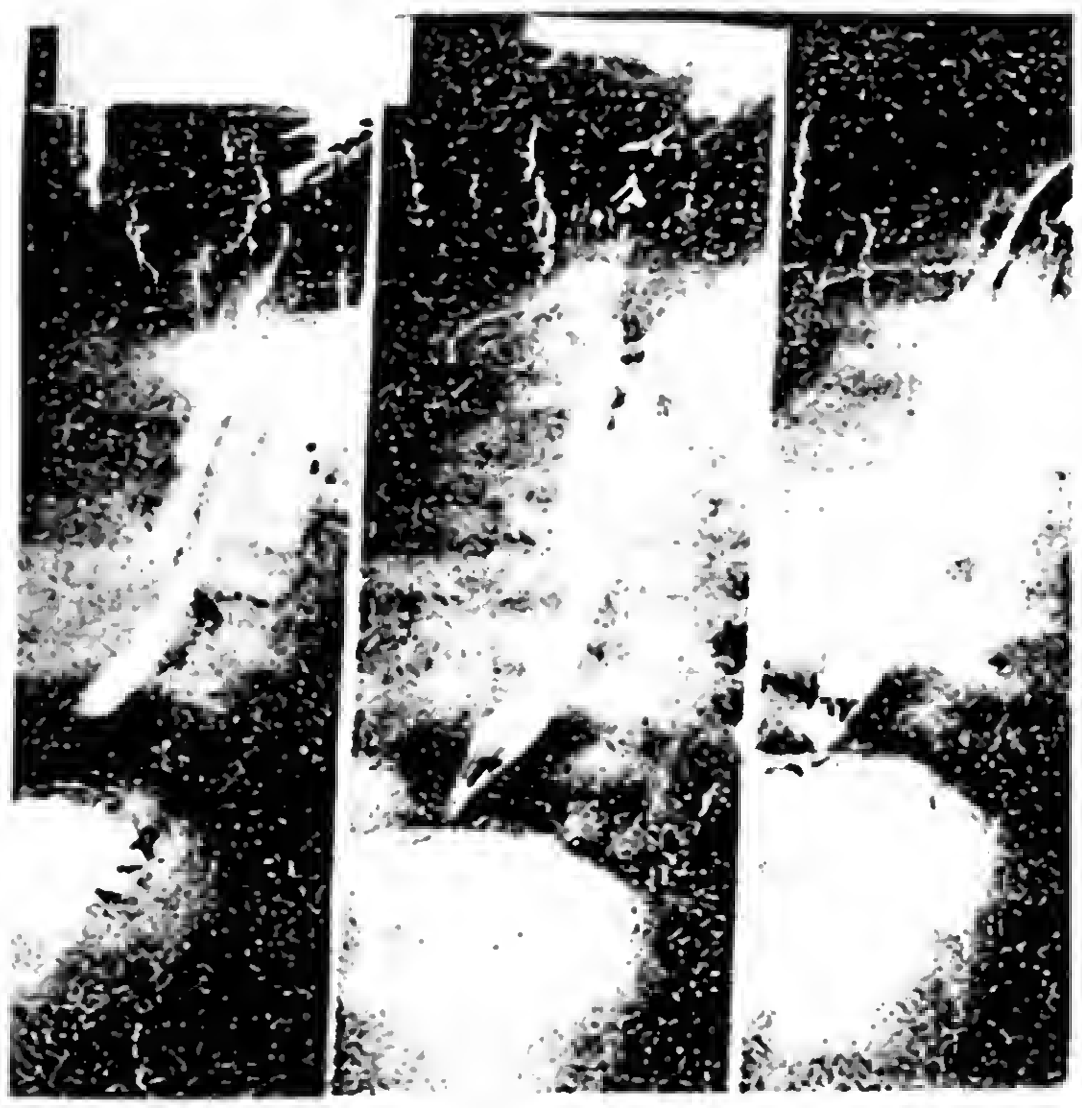
Research Letter

TRACHEO ESOPHAGEAL FISTULA AND ESOPHAGEAL ATRESIA

Atresia of the esophagus occurs with the incidence of 1 1 in 3000 to 5000 live births, in 80 to 90% cases it is associated with an abnormal communication (fistula) between the trachea and esophagus. Early diagnosis of tracheo esophageal fistual in the newborn baby needs a good deal of clinical experience and any delay in the diagnosis can lead to dangerous consequences in the baby.



Barium swallow showing H-Type TEF

We have diagnosed three babies with TEF in a period of two years. One of these underwent many investigations including many X-ray exposures, chest CT Scan, immunoglobulin electrophoresis, I antitrypsin level, screening for various infections without reaching a diagnosis. Clues to the correct diagnosis were[1] the very early onset of the problem[2]. Frequent choking and aspiration during feeding. Barium swallow was performed which showed H-type TEF (Fig-I).

Tracheoesophageal fistula from the incomplete fusion of the lateral walls of the primitive foregut to divide the posterior esophagus and the anterior trachea. Esophageal atreasia results from the defective growth of the entodermal cells of the foregut.

In more then 85% cases the fistula is between the distal esophagus and the airway. H-type constitutes 4% of TEF, less commonly the esophageal atresia and TEF may occur in an unusual combination.

Babies with esophageal atresia with or without TEF are often of low birth weight. Approximately 21% of these babies are premature and 19% are small for gestational age. Associated anomalies are seen in 30% cases including the syndrome of vertebral and vascular defects, imperforate anus, renal defects, some cardiac, genital and skeletal defects (VATER syndrome) as was the case with one of our patients who had TEF assoiated with verterbral defects, absence of right radius and abnormal genitalia. This patient was diagnosed in first few hours after birth. The third patient had an isolated TEF that was also diagnosed without any difficulty.

Polyhydramnios is common due to the high level of gastrointestinal obstruuction. Infants present in the first few hours of life with copious secretions, choking, cyanosis and respiratory distress. Diagnosis can be confirmed with chest X-ray after careful placement of a nasogastric tube to the point at which resistance is met. On chest x-ray, the tube will be seen in the blind pouch. If a TEF is present to the distal esophagus, gas will be seen in the abdomen.

If a fistula connects the proximal exophagus to the trachea, the first attempt at feeding may lead to massive aspiration. Infants with atreasia but no fistula had a scaphoid, airless abdomen.

In the H-type TEF, the usual presentation is recurrent aspirtion pneumonia and dignosis may be delayed for days or even months. The tracheal orifice of this type of fistula is easily detectable at bronchoscopy. Aspiration of pharyngeal secretions is almost universal patients with TEF, but aspiration of gastric contents via the distal fistula causes a more severe chemical pneumonitis.

Tracheo-esophageal fistual is a surgical emergency. The tube in the proximal pouch should be placed on continuous suction to drain secretions and prevent aspiration. The head of the bed should be evacavated to prevent reflux of gastric contents through the distal fistula into the lungs. Intravenous glucose and fluids should be provided and oxygen administered as needed. Definitive treatment is surgical and depends on the distance between the segments of esophagus.

Prongosis is determined primarily by the presence or absence of associated anomalies. Stenosis at the anastomotic site is common and may require dilatations. Persistent abnormal motility is always found in the distal esophagus; it predisposes to gastro-esophageal reflux, aspiration, oesophagitis and stricture formation.

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HYDATID CYST PRESENTING AS AN INTRACRANIAL SPACE OCCUPYING LESION

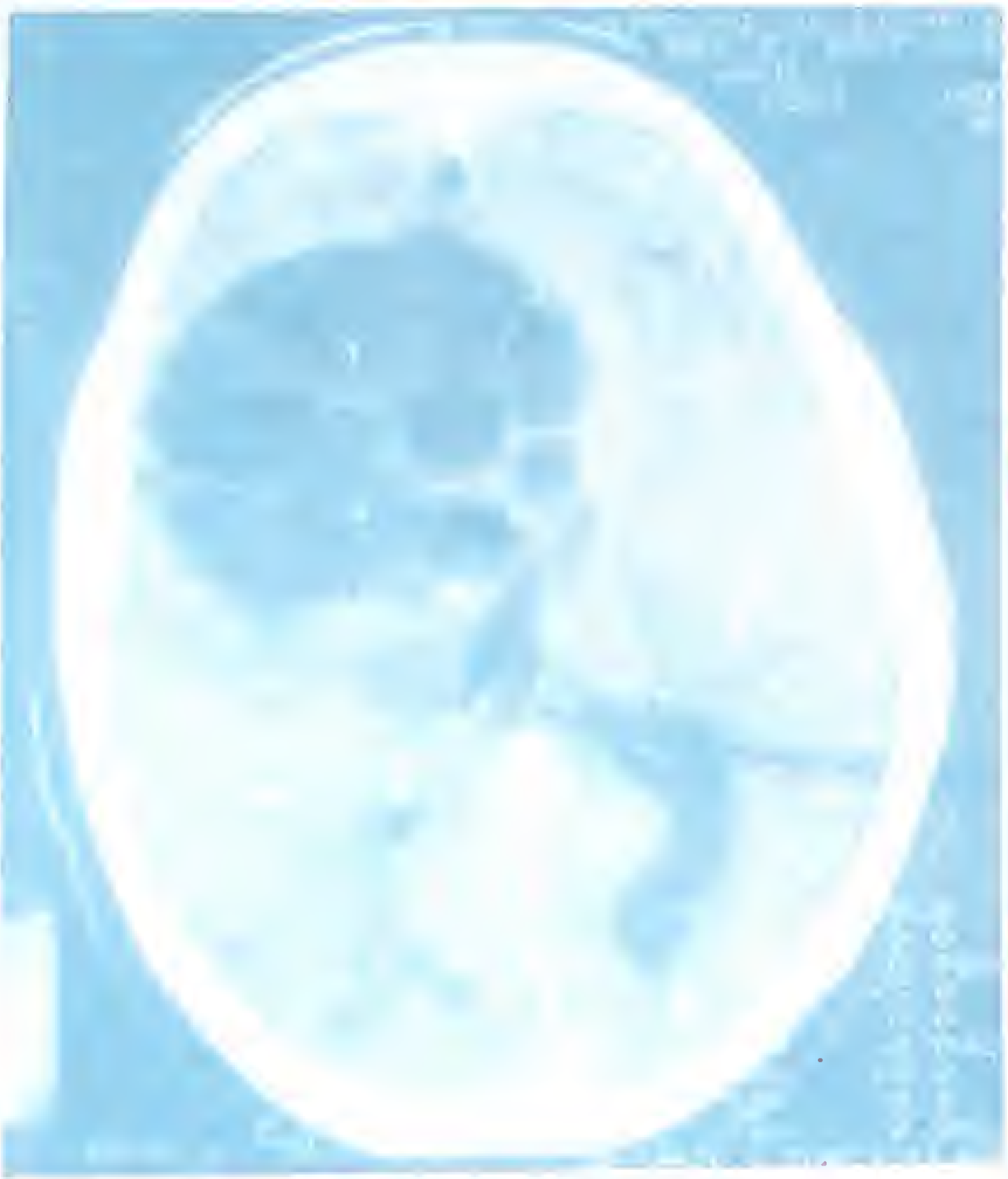
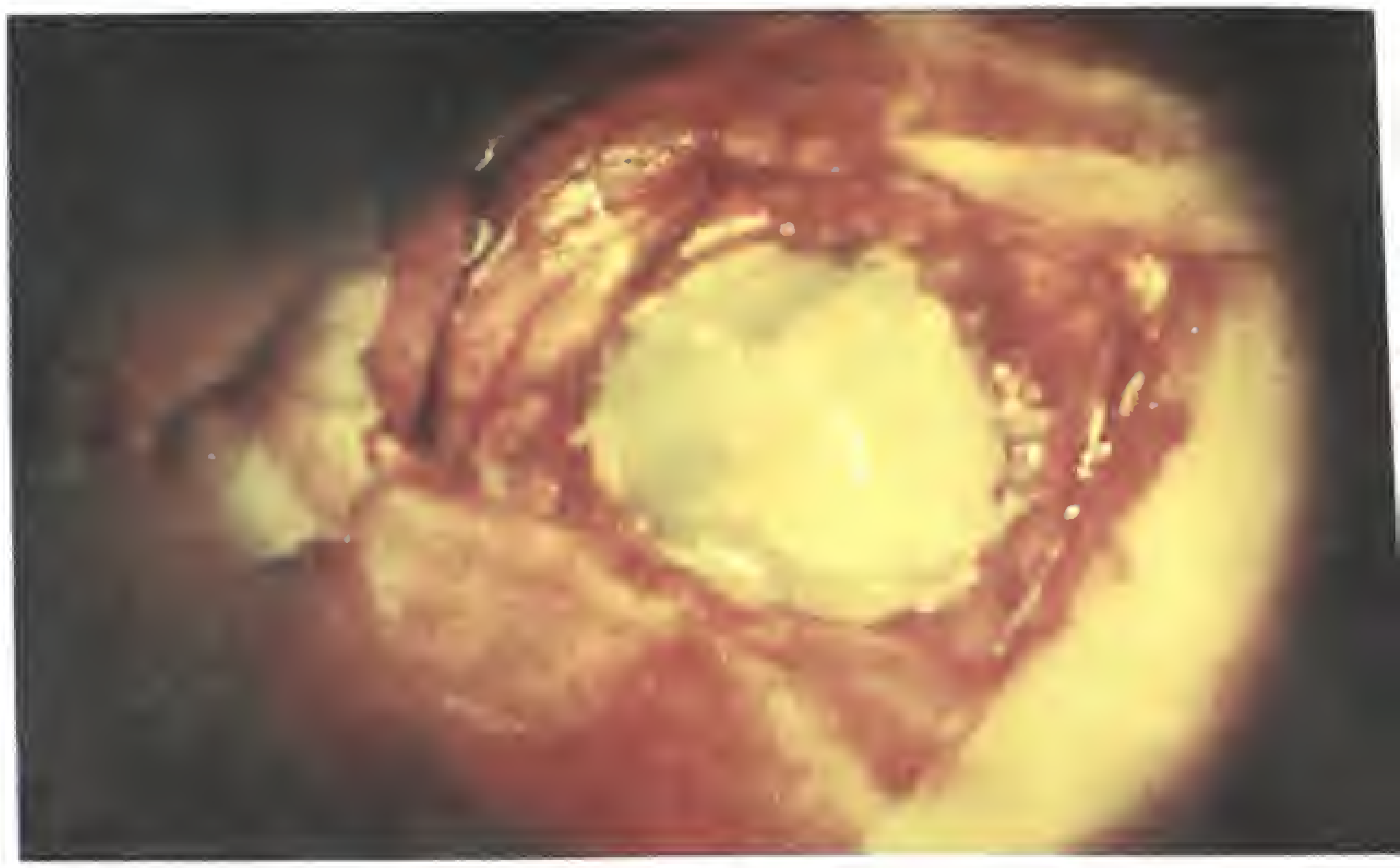


Fig.I



A 22 year old female from rural community presented with symptoms suggestive of raised intracranial pressure of six months duration. There was history of generalized Tonic-clonic seizures. The patient also complained of diminution of vision. Clinical examination revealed a healthy female with unremarkable general physical examination. She had minimal spastic hemiparesis on right side. Fundus showed early papilloedema. Laboratory investigations were within normal limits. X-rays of the chest and skull were reported to be normal. A computerised axial tomographic scan with contract enhancement demonstrated a multiloculated posteior frontal cystic space occupying lesion on the left side without any surrounding oedema of the brain (figure No.1). There was midline shift as well as the ipsilateral ventricular system was compressed. A presusmptive diagnosis of hydatid cyst of the brain was made. Ultrasound of abdomen was normal. Patient underwent a craniotomy. On opening dura underlying brain was tense. A small corticectomy revealed a sub cortical hydatid cyst. The cyst was decompressed and thirtyone daughter cysts were removed from within the mother ycst (fig. No.2). The mother cyst was also excised. Post operative recovery was uneventful.

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Commentary

LEPROSY - DIAGNOSTIC CHALLENGES IN THE NEW MILLENNIUM

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Leprosy, a chronic disease caused by an acidfast mycobacterium, mycobacterium leprae (M. Leprae) has plagued mankind since times immemorial. Egypt and other Middle East countries enjoy the dubious distinction of having introduced leprosy into the world. The occurrence of leprosy in Egypt dates back to as early as 2400 B.C. In India, the disease was known by the name of Kustha.

The last two decades have seen a rapid decline in leprosy case load throughout the world, the total number of patients having come down to around 1.2 million as against over 13 million in 1980. This decline in numbers has been due to wide application of Multidrug therapy (MDT)[1]. Not only has the prevalence rate come down, the profile of patients has also shown a shift towards early disease and fewer deformities among newly detected patients[2].

In clinical practice, leprosy is diagnosed clinically and to a limited extent, confirmed by the demonstration of acid fast bacilli (AFB) in skin smears. Now, with the significant drop in prevalence rates of leprosy, more intensive efforts, backed by newer techniques, will be required to face the emerging diagnostic and therapeutic problems.

Newer laboratory techniques will be needed for the following reasons:

a. To confirm the diagnosis in suspicious cases especially when the histopathological features are nonspecific.
b. To distinguish between reactions and relapses.
c. To identify potential or actual relapses.
d. To monitor treatment, i.e., activity, inactivity and resistance
e. To understand the transmission of the disease in the community. Hence, the following techniques are required.

A. Techniques to demonstrate M. Leprae or its components.

In the absence of in vitro cultivation of M. Leprae, the measurement of the bacteriological index (B1) in skin smears has been widely used to confirm the diagnosis and to monitor the progress of patients under treatment[3,4].

The newer techniques to demonstrate the components of leprosy bacillus are:

Chemical Methods

Structurally, M. Leprae has several characteristic lipids in its cell wall, notably mycolic acid and phenolic glycolipid-I.[5,6]

There are well established methods for their extraction and assay, e.g. thin layer chromatography (TLC), high performance TLC (HP-TLC) and high performance liquid chromatography (HPLC). New software programmes for quick identification of various mycobacteria using these lipid patterns on HPLC have also been developed. These techniques can be used to confirm the presence of M. Leprae-specific lipids in the tissues, but they have some limitations.

Immunological methods

During the last decade, several M. Leprae antigens have been expressed in gene libraries, some with epitopes for T cells and B cells, indicating their potential as future immunodiagnostic or immunoprophylactic agents.

Polyclonal and monoclonal antibodies targeting various common or specific antigens (epitopes) have been used. Targeting of antigens like the superoxide dismutase (SOD) enzyme, which has both conserved and specific epitopes, would be advantageous as their presence would imply active infection.[7,8]

Molecular biological techniques

Several specific gene sequences of M. Leprae been developed as gene probes for direct demonstration or amplification in various specimens (Skin or nasal smears, biopsies, tissue sections, blood etc.) from patients or healthy contacts. These probes are of various types[9,10].

i. DNA targeting probes.
ii. RNA targeting probes.
iii. Gene amplification methods: The highest sensitivity can be achieved with the polymerase chain reaction (PCR). Several PCR techniques to amplify different genes of M. Leprae have been developed during the last decade e.g. conventional DNA-based PCR,

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reverse-trascription PCR, nested PCR. These assays are sensitive up to the level of 1-10 organisms and are reported to be positive in 60-75 smear negative paucibacillary specimens.

B. Techniques to determine viability, drug susceptiblity or resistance.

Multiplication of M. Leprae in the footpads of normal mice and immuno compromised mice or rats has been extensively used in monitoring viability of M. Leprae and for drug screening. In recent years, numerous markers of viability of M. Leprae have been described and developed into in vitro techniques for drug screening and for monitoring the response to chemotherapy.

Methods based on morphological features such as morphological index, fluorescent diacetate-ethidium bromide (FDA-EB) staining, and laser microprobe mass analysis (LAMMA; based on the spectra of intercellular Na+/K+ratio) have been used to estimate the viability of M. Leprae from clinical specimens[11]. For drug screening the latter two methods have also been used as well as the Bactac system[12]. All these methods can only detect more than a million bacterial cells and, as such, are not suitable for most leprosy patients.

Some of the important newer methods are:

i. Bioluminescent techniques: ATP bioluminescence assays[13].
ii. Molecular methods for determination of viability and drug resistance- Polymerase chain reaction.

C. Techniques for eliciting strain differentiation for molecular epidemiology.

It was long believed that there were no strain variations in M. Leprae, but now these have been discerned by using molecular methods[14]. Some of these methods are:

i. Arbitrary primer amplification methods.
ii. Amplified ribosomal DNA finger printing.
iii. Strain specific probes.

To conclude in the coming decade PCR labs may be established even in smaller centres as their field application is not difficult if proper training is provided. Several of the above gene probes and PCR systems are likely to become available in kit forms. Hybridization with probes will become even easier with several nonradioactive detection systems becoming available. Demonstration of nucleic acids by way of a colour blot after extraction and hybridization/amplification from skin scrapings or biopsy specimens would be a definitive and sensitive method for detecting M. Leprae. In order to derive the maximum benefit, the established techniques should be integrated with the newer investigative techniques.

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ABDOMINAL TUBERCULOSIS

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Abdominal tuberculosis is an ancient disease. It is world wide in distribution widely prevalent in developing countries and even in the western world there has been a resurgence of the disease in recent years with the advent of AIDS. While abdominal tuberculosis is one of the common forms of extra-pulmonary tuberculosis and responsible for considerable morbidity and mortality in India, the exact prevalence is unknown, although in autopsy studies it has been reported to be 0.2-5.1%[1]. An incidence of $500/10^5$ has been reported from developing countries[2]. The frequency of the intestinal disease is related to the severity of the pulmonary involvement. Abdominal tuberculosis has been noted in 5-8% of cases with minimal lesions on chest radiograph compared to 14-18% with moderately advanced and 70-80% with far advanced pulmonary lesions[3]. However this can no longer be taken as a diagnostic tool because about 60-70% of patients have no evidence of pulmonary tuberculosis.

Tuberculosis may involve any part of the gut from the oesophagus to anus but the most common site of involvement is the distal ileum and ileocaecal region[4]. In abdominal tuberculosis, gastrointestinal involvement has been noted in 56.9%, peritoneal in 37.6% and mesentric lymphnodes in 6.2%[5]. The pathogenesis of intestinal tuberculosis is not known. Possible routes of infection include direct invasion by ingested organisms, haemotogenous seeding, transport by way of infected bile and extension from adjacent diseased organs or tissues. Three pathological varieties of bowel involvement are recognized-ulcerative, hypertrophic and mixed (ulcerohypertrophic) seen in 20%, 10% and 70% of patients respectively. Abdominal tuberculosis has non specific and protean clinnical manifestations. Females are affected slightly more frequetly and occurs at any age but mostly affects those in third and fourth decade of life. Majority of patients (60%) have a chronic presentation with duration of symptoms varying upto 10 years, 40% have acute presentation in the form of intestinal obstruction accounting for 3.4-11% of all small bowel obstructions; perforations accounting for 5-7% of all gastrointestinal perforations; simulating peritonitis and simulating appendicitis.[6]

Various symptoms in decreasing order of frequency are: abdominal pain, weight loss, fever, weakness, nausea, borborygmi, anorexia, vomiting, postprandial distress and distension, night sweats, constipation, diarrhoea, amenorrhea and haemorrhage[7]. Frank Malabsorption syndrome may occur in upto 20% cases of intestinal tuberculosis. Clinical examination reveals malnourished and chronically ill patient, vigrous peristalitic activity with distended bowel loops, muscle gaurding in patients with peritoneal involvement. An abdominal mass may be palpable in 30% of cases. Abdomen may feel doughy or ascites may be present. Other complications like internal and external fistulae, anusitis, perianal fissures and abscesses may be seen. Other clinical features depending upon the site of involvement of the gut may be present.

The Gold standard for the diagnosis of tuberculosis is isolation of Mycobacterium tuberculosis from the lesions or exudates. However, this is quite difficult and time consuming hence, indirect evidences like demonstration of characteristic tubercular granuloma have been considered diagnostic. Many a times, even pathological diagnoses may not be established due to inaccessibility of lesions using non-invasive methods and paucity of pathognomic lesions in intestine. Evidence of tuberculosis elsewhere in the body (lungs, lymphnode, endometrium etc.) in the presence of highly suspicious clinicoradiological features of abdominal tuberculosis is also considered useful for the diagnosis of abdominal disease[5,8]. Techniques for supportive diagnosis of abdominal tuberculosis includes radiography of chest, plain X-ray abdomen, contrast radiography, ultrasonography, computed tomography, immunodiagnostic tests and biochemical markers of tubercular infection X-ray chest and abdomen may reveal positive findings upto 30% only[9]. While contrast radiographic features are non-specific as similar findings may also be seen in other abdominal diseases.

CT scan with its ability to provide a comprehensive

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overview of abdominal structures is the imaging modality of choice for evaluation of abdominal tuberculosis[10]. Serological methods of diagosis have been recently developed including ELISA, soluble antigen fluorescent antibody test (SAFA) having specificity of over 90% and sensitivity of around 80% in abdominal tuberculosis. Adenosine deaminase estimation and y-interferon are another useful markers in diagnosing tubercular ascites having a sensitivity and specificity of over 95%[5,6].

Techniques for definitive diagnosis include histological diagnosis, demonstration of mycobacteria and some newer modalities of diagnosis. The tissues for histological diagnosis can be achieved by Laproscopy, colonoscopy, upper GI endoscopy and enteroscopy depending upon the site of gut involvement. Demostration of tubercle bacilli from clinical samples is the most direct evidence of the disease. However, the yield of smear examination is poor on Ziehl Neelson stainning and take 4-6 weeks. Presently rapid culture techniques (Radiometric Bactec, Septi Check and microcolony) have reduced culture time to 2 weeks. The organism can be grown from endoscopic biopsies, operative biopsies, ascitic fluid and fine needle aspiration from tubercular mass lesions. Newer modalities of definitive diagnosis include DNA probe, DNA amplification using PCR, RNA amplification and Firefly luciferase. However, such modalities are expensive and can be performed only in specialized centers. Treatment of abdominal tuberculosis is medical and surgical. Medical treatment includes the conventional anti tubercular drugs used for other forms of tuberculosis also. The duration is usually 9-12 months although 6 months short course chemotherapy has been used successfully[11]. Surgery is indicated for specific complications like obstruction, perforation, fistula repair, GI bleed.

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UPDATE IN NEUROLOGY

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Advances in neurology in the past 2 years have focused on a variety of basic issues, including migraine headache, stroke, neuroimaging, degenerative diseases, neurologic aspects of medical conditions, and seizure disorders.

Migraine Headache

Patients with migraine headaches often have difficulty explaining their suffering. In the physician's office, the typical patient places the heel of the hand in one orbit and the fingers up over the forehead, all in the first division of the fifth cranial nerve. Migraine pain is actually pain that is referred into the first division of the trigemial nerve, and it is probably due to a abnormality in the way in which the central nervous system processes nociceptive information.

Promotility Agent Was Effective in Treatment

Tfelt-Hansen P, Henry P, Mulder IJ, et all. The effectiveness of combined oral lysine acetylsalicylate and metoclopramide compared with oral sumatriptan for migraine. Lancet, 1995;346:923-6.

Sumatriptan has become a commonly used agent for migraine headaches. It is expensive, however, and patients often delay taking a drug that costs as much as $35 a dose. The injectable form is difficult for some patients to take, and the nasal form is poorly absorbed and leaves a bitter after taste. The oral drug is poorly absorbed because migraine attacks also cause gastric stasis and therefore decrease absroption of all oral drugs.

In this clinical trial, Tfelt-Hansen and colleagues assessed the efectiveness of salicylates (the class of drug most commonly used for migraine) plus a promotility agent. They randomly assigned 421 patients with migraine to receive metoclopramide, 10 mg, followed by lysine acetylsalicylate (equivalent to 900 mg of aspirin); oral sumatriptan (100mg); or placebo. In 57% of patients receiving the combined regimen, 53% of those receiving sumatriptan, and 24% of those receivig placebo, the intensity of headache decreased from severe to mild or absent.

This study makes a critical point about the treatment of migraine: Simple oral medication alone is relatively ineffective. A promotility agent plus aspirin performed at least as well as the most expensive drug available. Another effective drug is indomethacin, which is given by suppository and crosses the blood-brain barrier. This is an effective and commonly used agent in Europe but has not become popular in the United States[1]. Indomethacin suppositories contain 50 mg of the drug. Because many headaches recur, I instruct patients to cut a 50 mg indomethacin suppository into thirds and insert them every 10 to 15 minutes as necessary. For patients who decline to use suppositories, a basic oral analgesic following a dose of metoclopramide is a reasonable second choice that is much less expensive than most alternatives. Two new drugs, zolmitriptan and naratriptan, are now available, but they offer little advantage over previously available medications because they are avilable only in oral preparations.

Divalproex Sodium Seemed to be Effective Prophylaxis

Silberstein SD. Divalproex sodium in headache: literature review and clinical guidelines. Headache 1996;36:547-55.

For patients with severe or frequent migraine attacks, propranolol and amitriptyline are frequently used as prophylaxis. Many other agents have been shown to decrease the frequency and intensity of migraine attacks (Table 1).

In this nonsystematic review, Silberstein cited all clinical studies of divalproex sodium (sodium valproate plus valproic acid) used as prophylaxis agents migraine. Valproic acid, a standard antiseizure medication, is presumed to exert its effects by facilitating the action of the neurotransmitter Y-aminobutyric acid (GABA). In reviewing four small, randomized clinical trials, Silberstein found that divalproex sodium greatly improved the headache indices in 75% to 87% of patients. In general, headache frequency decreased by about 50% in patients receiving divalproex sodium and by about 10% to 15% in patients receiving placebo. Divalproex sodium seemed to be slightly more effective than propranolol.

Although the studies were small and larger ones are needed, valproic acid, generally prescribed as divalproex sodium, seems to be a good choice for migraine

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Table-1: Drugs Used for Migraine Prophylaxis

Drug	Daily Dose, mg	Common Adverse Effects
Amitriptyline	10-150	Sedation, dry mouth, constipation, weight gain, hypotension, urinary retention.
Aspirin	650-1950	Dyspepsia; gastrointestinal bleeding.
Cloridine	0.2 - 0.6	Dry mouth, sedation, headache, constipation.
Cyproheptadine	12-20	Sedation, dry mouth, dyspepsia.
Divalproex sodium	250-750	Gastrointestinal symptoms tremor, sedation, temporary alopecia, weight gain, rashes, elevated aminotransferase levels, hematologic dysfunction.
Erogonovine maleate	0.6-2	Nausea, vomiting, abdominal pain, diarrhea.
Fluoxetine	20-60	Anxiety, insomnia, sweating, tremor, gastrointestinal symptoms.
Impiramine	10-150	Sedation, dry mouth, constipation, weight gain, hypotension, urinary retention.
Methysergide	4-8	Gastrointestinal symptoms, weight gain insomnia, edema periphegal vasoconstriction, retroperitoneal and pleuropulmonary fibrosis, fibrous changes in heart values.
Propranolol	80-240	Fatique, lassitude, depression, insomnia, nausea, vomiting constipation.
Sertraline	50-200	Anxiety, Insomnia, sweating tremor, gastrointestinal symptoms.
Verapamil	80-160	Headache, hypotension, edema, constipation, atrioventricular heart block.

prophylaxis. It appears to be at least as effective as and better tolerated than B-blockers or tricyclic antidepressants. However, valproic acid may cause weight gain and hair loss and should not be used by women who may become pregnant. This contraindication could be a serious clinical problem because many patients with migraine are young women.

Stroke

Stroke remains a leading cause of death and disability in the United States. Recent advances in treatment include thrombolytic therapy given within 3 hours after onset of ischemic stroke. Early studies also indicate that blockage of glutamate, an excitatory neurotransmitter, reduces the sensitivity of central neurons to ischemia; however, no glutamate-blocking drugs are clinically avialable. These therapeutic advances have reinvigorated clinical investigation of stroke.

Transesophageal Echocardiography Outperformed Transthoracic Echocardiography

Rauh R, Fischereder M, Spengel FA. Transesophageal echocardiograppy in patients with focal cerebral ischemia of unknown cause. Stroke. 1996;27:691-4.

These onset of stroke due to occlusive vascular disease, or thrombosis, is stepwise or progressive ("stuttering" onset). This type of stroke often occurs while the patient is sleeping. Embolic strokes usually are sudden in onset and produce maximum neurologic deficits at the outset. A patient presenting with stroke usually undergoes computed tomography to rule out bleeding and undergoes carotid Doppler studies to detect severe stenoses, which can be repaired surgically. However, when patients have neither a hemorrhagic stroke nor evidence of carotid stenosis, the rest of the diagnostic evaluation is controversial.

Rauh and colleagues assessed the usefulness of transesophageal echocardiography in patients with cerebral ischemia of unknown causes. Thirty consecutive patients who had completed strokes were enrolled. All patients were in sinus rhythm, had no cardiac disease known to be linked to the occurence of cardiogenic emboli, had minimal carotid artery stenosis, and were evaluated by transthoracic and transesophageal echocardiography.

Transthoracic echocardiography yielded abnormal findings in 6 patients, but no embolic source was found. Transesophageal echocardiography identified thrombus in the left atrial appendage in 3 patients, atrial septal aneurysm in 2, and patent foramen ovale in 7. It also disclosed aortic plaques in 19 patients. The use of transesophageal echocardiography prompted a change of therapy in 3 of the 30 patients.

Transesophageal echocardiograpy is thus the test of choice for evaluating patients suspected of having embolic strokes. Compared with dual-helical computed tomography, an expensive test that is not always available, transesophegeal echocardiography has a sensitivity of 87% and specificity of 82%. Thus, it is 3 to 6 times more accurate than transthoracic echocardiography. It is a safe test; only 1 person died among 10000 tests, and this patient had undiagnosed esophageal cancer. Because of its ability to detect patent foramen ovale, the technique also precludes the need for venography or other studies to look for deep venous thrombi.

Many patients do not require transthoracic or transesophgeal echocardiography. Patients who will receive anticoagulants (such at those with atrial fibrillation or dilated cardiomyopathy) do not need this study. Similarly, if a decision has been made not to use anticoagulation, no study is necessary. As with all tests, transesophageal echocardiography should be used only in patients whose therapy may be altered as a result of the test.

Evidence Linked Alzheimer Disease to Hemorrhagic Stroke

Greenberg SM, Briggs ME, Hyman BT, et al. Apolipoprotein E_B *4 is associated with the presence and earlier onset of hemorrahage in cerebral amyloid angiopathy. Stroke. 1996;27:1333-7.*

Intracerebral hemorrhage has historically resulted from hypertension. In such strokes, the source of bleeding is small vessels in the putamen and other areas in the deep brain. Despite aggressive treatment of hypertension, however, cerebral hemorrhage has remained nearly as common as in the past. The reason is the increased frequency of cortical hemorrhages. This type of hemorrhage may result from extension of a hypertensive hemorrhage, trauma, hemorrhagic transformation of an ischemic infaraction, hemorrhage of a tumor, or cerebral vascular malformation.

A growing cause of hemorrhage in the cortex or gray or white matter is amyloid angiopathy, which leads to small and sometimes multiple hemorrhages. Risk of Alzheimer disease. because apolipoprotein Ee4 is associated with a family risk for Alzheimer disease, Greenberg and colleagues sought to determine whether this allele is associated with amyloid angiopathy. They identified 27 patients who presented with cerebral lobar hemorrhage and had a high probability of amyloid angiopathy. These patients were compared with 1899 elderly patients from a population-based sample and 18 patients with deep cerebral hemorrhage that was characteristic of a hypertensive mechanism.

Patients with multiple lobar hemorrhage had a twofold increase in frequency of the apolipoprotein E e4 allele compared with the general populaltion sample. patients who carried the e4 allele and sustained lobar hemorrhages were more than 5 years younger than those without the allele who sustained lobar hemorrhages.

The clinical message from this study is not completely clear, but the results should cause clinicians to at least consider age and Alzheimer disease as risk factors for adverse effects of warfarin. However for most patients who are at risk because of thromboembolic disease, including stroke, the benefits of warfarin still far outweigh its risks. At this stage of our knowledge, the routine use of a test for the apolipoprotein E e4 allele is not warranted.

Screening for Asymptomatic Bruit Had Poor Cost-Effecxtiveness

Lee TT, Solomon NA, Heidenreich PA, et al. Cost-effectivenness of screening for carotid stenosis in asymptomatic persons. An Intern Med. 1997;126:337-46.

A common clinical scenario is an asymptomatic bruit. In the Asymptomatic Carotid Artery Study (ACAS), a 5-year randomized clinical trial of patients with asymptomatic bruit, those with stenoses greater than 60% had a 53% reduction in the risk for ipsilateral stroke if they underwent endarterectomy done by skilled surgeons compared with patients treated with anticoagulants only[2].

Lee and colleagues performed a cost-effectiveness analysis on patients in clinical trials who matched the characteristics of those in ACAS. The analysis used the following assumptions: Screening would be done by ultrasonography, and angiography would be done on patients with at least 60% stenosis on ultrasonography. Because stroke occurs more often in men, the analysis included men only. Patients with clinical evidence of carotid artery disease were excluded from screening programs.

The authors found that under these conditions, identification of patients who had asymptomatic carotid artery stenosis of at least 60% and would then undergo surgery would cost $120,000 per quality-adjusted life-year. Under the most favourable assumptions (in which the screeing test was perfect and the prevalence of disease among persons screened was 40%), the marginal cost would decrease to $50,000 per quality-adjusted life-year. For hypertension, cost estimates for screening and treatment are about $12,000 to $43,000 per year of life saved (1993 U.S dollars), and coronary artery by-pass grafting (CABG) for patients with left main coronary artery disease costs $6300 to $7000 per quality-adjusted life-year (1991 U.S. dollars). Many experts believe that interventions costing more than $100,000 per quality-adjusted life-year are not cost-effective. However, this is an arbitrary value judgment that could conflict with a physician's ethical responsibility to the individual patient rather than the economic benefit of society at large.

Much of the cost is incurred because the typical patient with carotid artery disease tends to be an approximately 70-year-old man with coronary artery disease. These results may therefore underscore what clinicians already know intuitively: that patients with many comorbid conditions may not be good candidates for endarterectomy. However, clinicians do deal with individual patients; thus, despite these results, patients who are relatively healthy and who have asymptomatic carotid artery disease should undergo endarterectomy, as demonstrated by ACAS. No available technology predicts when a stroke wil occur in patientrs with carotid artery stenosis. However, one can assume that if no other disease kills a patient with carotid stenosis, a stroke will eventually occur if surgery is not done.

Neuroimagig

Most patients who present to emergency departments with symptoms of stroke undergo noncontrast computed tomography, to rule out bleeding as a cause. Once this test is done, many physicians do no further brain imaging studies; instead, they focus on treating the underlying causes of thrombotic or embolic stroke. With the advent of more intensive therapies that are effecive only in a narrow window of time, new imaging techniques are becoming useful.

Diffusion-Weighted Magnetic Resonance Imaging Detected Early Ischemia

Lutsep HL, Albers GW, DeCrespigny A, et al. CLinical utility of diffusion-weighted magnetic resonance imaging in the assessment of ischemic stroke. Ann Nerurol. 1997;41:574-80.

SInce the introduction of thrombolytic therapy for acute stroke, advance groups such as the American Heart Association have promoted the concept of "brain attack" to the public. Analogous to heart attack symptoms, brain attack symptoms should prompt a patient to an emergency department as rapdily as possible. Thrombolytic therapy is most efficacious if given within 3 hours of symptom onset[3]. Unfortunately, patients often arrive at the hospital aphasic, so the exact time of symptom onset cannot be determined. In these cases, thrombolysis is not offered because the risks mighty outweigh the benefits.

Diffusion-weighted magnetic resonance imaging (MRI) detects the diffusion of water molecules associated with cytotoxic edema. It has been shown that diffusion-weighted MRI can detect brain ischemia before standard MRI can[4]. In a retrospective analysis, Lutsep and colleagues reviewed 103 diffusion-weighted MRI studies of patients with stroke symptoms to determine the clinical usefulness of the test.

Diffusion-weighted MRI was done within 24 hours of stroke in some third of patients. It aided in diagnosis or management in 8% of patients. Unfortunately, because the earliest study was performed 5 hours after onset of symptoms, this study could not determine whether diffusion-weighted MRI will help to identify patients in the 3 hours window in which thrombolysis is moist beneficial.

Diffusion-weighted MRIs not yet ready to become part of routine practice, but it probably will be soon. It holds great promise for identifying patients who will benefit most from thrombolytic therapy.

Degenerative Diseases

Most neurologic advances in the past 2 years have been made in the area of parkinsonism and other neurodegenerative conditions. Surgical approaches have become a clinical option for patients with severe Parkinson disease. Three therapeutic options are now available for patients with multiple sclerosis.

Surgical Treatments Emerge for Symptom Control in Parkinson Disease

Lang AE, Lozano AM, Montgomery E, et al. Posteroventral medial pallidotomy in advannced Parkinson's disease. N Engl J Med. 1997;337:1036-42.

Parkinson disease occurs most commonly in persons 45 to 65 years of age. Degeneration of the substantia nigra causes a depletion of dopamine and an imbalance between dopamine and other neuro-transmitters, such as acetylcholine, that are normally present in the corpus striatum. Medical treatment attempts to correct this imbalance by blocking the effect of acetylcholine with anticholinergic drugs or by using levodopa, the precursor of dopamine. In a poignant account of living with Parkinson disease, the author describes the results of pallidotomy, a surgical therapy[5].

Pallidotomy is a stereotactic operation that attempts to destroy the motor portion of the globus pallidum, a part of the basal ganglia that secretes neurotransmitters that oppose dopamine. Lang and colleagues studied 40 patients with severe Parkinson disease who underwent pallidotomy. Patients had either disabling immobility or dyskinesias from levodopa therapy. Approximately half of the patients who had been depended on assistance in activities of daily living before surgery became independent for 6 months afterward. However, this improvemetn was not sustained over a 2-year period. Until prospective clinical trials are conducted, this study presents the best evidence that pallidotomy is an effective short-term treatment for patients with severe motor symptoms due to Parkinson disease or from the complications of pharmacologic treatment.

Another surgical intervention for parkinsonism is deep-brain stimulation[6]. During this procedure, high-frequency electrodes are placed in the globus pallidus. The electrodes imitate a lesion but do not kill the cells. Patients with these stimulators can turn them off and on to accomplish specific motor tasks. For example, by placing a magnet over a battery pack placed in the chest wall, a patient with a severe tremor can stop the tremor long enough to sign a check. During sleep, the device is kept off to avoid permanent brain damage. No formal clinical, trials have yet been done, but the technique seems promising.

The third surgical treatment is brain tissue transplantation. Surgeons can take cells from the substantial nigra of a fetus and stereotactically palce them into the striatum of a patient with parkinsonism. These cells are not rejected, and they secrete dopamine. However, the technique has two major problems. The first is ethical: Is it right to use cells from a fetus, even a dead fetus, to treat patients who are at least middle-aged? If the answer to that question is "yes," we then face the problem of insufficient numbers of fetuses to treat a disease as common as parkinsonism—the prevalence is about 15% in persons 65 to 74 years of age and more than 50% in those 85 years of age and older[7]. The ultimate solution, short of preventing the disease, may come from genetic engineering by which dopaminergic cells might be grown in culture.

Options for Treatment of Multiple Sclerosis Increase

Rudick RA, Cohen JA, Weinstock-Guttman B, et al. Management of multiple sclerosis. N Engl J Med. 1997;337:1604-11.

Multiple sclerosis is a common disease in young people marked by physical decline that usually occurs over 30 to 40 years. Before 1984, diagnosis was based on clinical signs and symptoms, but MRI has become a test with reasonably good specificity. Most patients have the relapsing-remitting from of disease, in which they are stable for long periods and then have epidodes of acute excerbations.

In this réivew, Rudick and colleagues discussed four therapeutic options, mainly for relapsing-remitting multiple sclerosis. For exacerbations, short-term high-dose corticesteroid therapy significantly accelerates recovery from acute symptoms. In patients with relapsing-remitting disease, interferon Bib, interferon-BIb, and glatiramer acetate (a mixutre of polypeptides) each produced about a one-thrid reduction in relapses compared with placebo.

Despite these advances, many questions about treatment remain: When should therapy be started? How long should therapy be continued? What are the mechanisms of action of the drugs? What are the long-term benefits? Answers to these questions are still guesses.

Neurologic Aspects of Medical Disease

Many clinical problems in neurology are complications of medical diseases or treatments. For example, hyponatremia, which can produce neurlogic symptoms, frequenctly occurs in patietns who have recently had surgery. The cause of this phenomenon was reviewed in the recent Update in Nephrology[8].

Major Events Occurred in more than 6% of patients hving routine Coronary Artery Bypass Grafting

Roach GW, Kanchuger M, Mangannno CM, et al. Adverse Cerebral outcomes after coronary bypass surgery. Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation Investigators. N Engl J Med. 1996;335: 1857-63.

More than 800 000 myocardial revascularization operations are performed annually throughout the world. One of the most common complications is neurologic dysfuncltion, including encephalopathy and stroke. Many observational studies have reported on a wide range of these complications, but the actual neurologic risk has been unknown.

Table-2: Risk Factors for adverse Neurologic Events in Patients Undergoing Elective Coronary Artery Bypass Grafting*

Risk Factor	Adjusted Odds Ratio+	
	Type I Neurologic Outcome	Type 2 Neurologic Outcome $
Proximal aortic atherosclerosis	4.5	
History of neurologic disease	3.2	
Use of intra=aortic balloon pump	2.6	
Diabetes mellitus	2.6	
History of hypertension	2.3	
History of pulmonary disease	2.1	2.4.
History of unstable angina	1.8	
Age (peradditional decade)	1.8	2.2
Systolic blood pressure >180mm Hg at admission		3.5
History of high alcohol consumption		2.6
History of previous coronalry artery bypass graft		2.2
Dysrhythmia on day of surgery		2.0
Antihypertensive therapy		1.8

* Date obtained from Roach GW, Kanchuget M, Mangano CM, et al. Adverse cerebral outsomes after coronary bypass surgery. Mulicenter Study of Perioperative Ischemia Research Group and the Ischemia Researcha dn Education Foundation Investigations. N Engl J Med 1996;335:1857-63.

+ $P< 0.05$ for all factors listed.

# Stroke, transient Ischemic attack, hypoxic encephatopathy, stupor, or come at time of discharge or death.

$ New deterioration in intellectual function, confusion, agitation, disorientation, memory deficit, or seizure without evidence of focal injury.

Roach and colleagues sought to determine the incidence and predictors of major perioperative adverse neurologic events and the use of resources associated with these events. In a multicenter prospective study, they followed 2108 patients under going elective CABG to monitor the development of two types of neurologic complication: focal injury, stupor, or coma at discharge (type I) and deterioration of intellectual function, memory deficit, or seizures (type 2).

These major adverse neurologic complications occurred in 6.1% of patients: type-I complications in 3.1% of patients (including 8 patients who died of stroke), and type 2 complications in 3.0%. Patients with neurologic symptoms had about an eight-fold higher risk for death, a more than twofold greater length of stay, and a fivefold higher rate of discharge to skilled nursing facilities compared with those without neurologic complications. Risk factors for complications are shown in Table 2.

Some decrease in neuropsychological function has been reported in up to one third of patients placed on extracorporeal circulation for any reasons[9]. Roach and colleagues study is worrisome because it brings into sharp focus the substantial rate of major neurologic complications sustained by patients undergoing CABG. Because CABG is so common, internists should use extra caution in referring patients with risks for these complications, which may trade one disease for another and could result in substantial suffering.

Incidence of Haemophilus influenzae Meningitis Decreased 93%

Schuchat A, Robinson K, Wenger JD, et al. Bacterial meningitis in the United States in 1995. Active Surveillance Team. N Engl J Med. 1997;337:970-6.

Until recently, bacterial meningitis occurred in 10000 to 20000 Americans each year[10]. Five pathogens were responsible for more than 80% of all cases: *Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitidis*, group B streptococci, and Listeria monocytogenes. In the 1980s, bacterial meningitis was primarily a disease of infants, with H. influenzae accounting for 79% of all cases. By 5 years of age, about 1 in 200 children had H. influenzae meningits.

By 1990, routine vaccination of infants against H. influenzae type b had become commonplace. This surveillance team measured the effect that the vaccine has had on bacterial meningitis by comparing data from 1986 with data from 1995. Summary results are shown in Table 3.

Since the introduction of the vaccine, the number of cases of meninngitis reported to have been caused by the five major pathogens decreased from 12920 in 1986 to 5755 in 1995. Nearly all of that decline has been due to the reduction in H. influenzae-related disease among children. The median age at which bacterial meningitis occurs increased from 15 months in 1986 to 25 years in1996, again because of the 93% reduction in the number of cases of H. influenzae meningitis.

In the United States, bacterial meningitis is now primarily a disease of adults. This is not true for most of the rest of the world. In the United States, how ever, the ranks of the most common causes of meningitis have changed radically; clinicians should take this into account when choosing empirical therapy.

Table 3: Incidence of the Five Common Causes of Bacterial Meningitis in the United States | 1986 and 1995*

Pathogen	Case of Bacterial Meningitis Per 100,000 persons	
	1986	1995
	n	
Haemophilus influenzae	2.9	0.2
Streptococcus pneumoniae	1.1	1.1
Neissaeia meningitidis	0.9	0.6
Group B streptococci	0.4	0.3
Listeria monocytogenes	0.2	0.2

* Data obtained from Schuchat A, Robinson K, Wenger JD, et al. Bacterial meningitis in the United States in 1995. Active Sureillance Team. N Engl J MEd. 1997;337:970-6.

Seizure Disorders

The management of seizure disorder was relatively straightforward until the 1990s. In the past 4 years, the U.S. Food and Drug Administration has approved five new drugs for use against partial scizures. The most recent is tiagabine. Other antiepileptic drugs and their relative costs are listed in table 4.

Newer Drugs were equally effective among themselves

Marson AG, Kadir ZA, Chadwick DW. New antiepileptic drugs: a systematic review of their efficacy and tolerability. BMJ. 1996;313:1169-74.

At least eight drugs are available for treating seizure disorders. The obvious questions is, which are most efficacious? Marson and colleagues evaluated the efficacy and tolerability of the newly developed antiepileptic drugs gabapentin, lamotrigine, tiagabine, topiramate, vigabatrin, and zonisamide in patients with refractory partial epilepsy. They systematically reviewed 20 published and 8 unpublished randomized, controlled trials of add-on treatment in 3883 patients.

All drugs were found to be superior to placebo in suppressing seizures, but none was more effective than any other. The results lead no two conclusions. First, older drugs—valproate and phenytoin—are still the best studied and are the first-line drugs to use against partial seizures. Second, new drugs with little or no improved efficacy should be used with great caution. Felbamate was the first of the newer drugs approved in the United States for use against partial seizures. When felbamate was finally released in 1993, the U.S. Food and Drug Administration was criticized for being too slow in approving the new antiepileptic agents, many of which were being sold in Europe. These criticisms were made despite the report that felbamate was associated with agranulocytosis at a rate 1000 times that of carbamazepie. Curiously, physicians in practice have remained hesitant to use carbamazepine because of early case reports of agranulocytosis, even though it is now a well-studied drug. However, sales of newer drugs, including felbamate, have done well even among general internists.

This is not to say that new drugs should not be used, but it seems only reasonable to favour drugs that have been well tested and have been shown to be effective and well tolerated. For the most part, the older antiepileptic agents fit these criteria. The new drugs do have a place; in msot cases, however, only specialists in seizure disorders should be using them, and thenn only in patients in whom older drugs have not controlled the seizures.

To sum up, the drugs of choice for partial seizures remain valproate and phenytoin. For generalized seizures, valproate should be the first choice followed by phenytoin or carbamazepine.

Table-4: Drugs Commonly used for Seizure Disorder and their relative Costs*

Drug	Daily Dose mg	Relative Cost $
Carbamazepine	800-1600	3
Felbamate	2400-3600	23
Gabapenitin	900-3600	19
Lamotrigine	300-500	22
Phenytoin	300-400	1
Tiagabine	32-56	21
Topiramate	2200-400	31
Valproic acid	1000-3000	3

* Data obtained from reference 11.

Relative cost estimates are wholesale prices and are relative to cost of generic phenytion.

Treatment of Status Epilepticus is Becoming Simpler

Lowenstein DH, Alldredge BK. Status epilepticus N Engl J Med. 1998;338:970-6.

Status epilepticus (continuing or rapidly recurring seizures) occurs in up to 150 000 persons per yearr killing about 55000 of them. Up to one third of adults with new-onset seizures present with status epilepticus. In general, single seizures last for about 60 seconds, and few last more than 120 seconds. Most practitioners know that therapy becomes urgent after about 20 minutes of seizure activity. Their estimates are hindered, however, because most medical histories come from the patients families who vastly overestimate the length of a seizure.

The main goal of Lowenstein and Alldredge review was to develop an approach to the management of status eiplepticus. The message was clear Treatment is getting simpler. After ensuring that life support measures are taken and glucose and thiamine given, one should begin with intravenous phenytoin, 20 mg/kg of body weight at a rate of 5 mg/min. Fosphenytoin is now available and may administered at the same dose as phenytoin. The apeutic blood levels may be reached sooner with fosphenytoin, but the major advantage of the drug is that, unlike phenytoin, it does not result in local tissue damage at the infusion site; this complication is caused by the diluent in which phenytoin is dissolved. The greater expense of fosphenytoin, however, may outweigh the benefits of the drug. Most advocate using lorazepam or another benzodia epine, but there are good reasons to avoid the later: Phenytoin is an excellent anticonvulsant, and benzodiazepines sedate consciousness and depress respiration. (A common joke among neurologists is "if you're nervous enough to feel you have to use diazepam, then it is probably more helpful for the patient if you give it to yourself.") If a benzodiazepine is used, lorazepam is a reasonable choice because its half-life is relatively short. Phenobarbital is given for seizures that continue after the phenytion infusion. If phenobarbital fails, general anesthesia should be administered.

Status epilepticus is life-threatening, and, like most life-threatening emergencies, it is a crisis that responds well if simple maneuvers are carried out in a clam, deliberate manner.

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DR. FAYAZ A. SHAWL

M.D., F.R.C.P., F.A.C.P., F.A.C.C.

Dr. Shawl currently is the Director of Interventional Cardiology at Washington Adventist Hospital, Takoma Park, Maryland, Director of Cath Lab and Interventional Cardiology at Prince George's Hospital Center, and is a Clinical Professor of Medicine at George Washington School of Medicine, Washington DC.

Dr. Shawl received his medical degree from Kashmir Medical College in 1972 and then completed his residency in England.

In 1977 Dr. Shawl moved to the United States and completed his Cardiology fellowship at The Walter Reed Army Medical Center. Dr. (Maj.) Shawl brought the military into the balloon age when he performed the first PTCA at a US military hospital. Between 1979 and 1990 Dr. Shawl retained clinical appointments at Georgetown University Schooll of Medicine, George Washington University School of Medicine and the Uniformed Services University School of Medicine, while developing leadership roles in Interventional Cardiology at both Washington Adventist Hospital and Prince George's Hospital Center.

Dr. Shawl is a Member of the American College of Physicians, the Royal College of Physicians of the United Kingdom, General medical Council of the United Kingdom, the American Medical Association and American Heart Association. He is a Fellow of the American College of Cardiology, the American College of Chest Physicians, American College of Physicians, The American College of Angiology and The Society for Cardiac Angiography and Interventions.

Dr. Shawl performed the first PTCA in the United States Army in 1980; Since then he has continued to be an innovator in all aspects of Interventional Cardiology. He developed a percutaneous approach ("Shawl Technique") to cardiopulmonary bypass support in "High Risk Angioplasty Patients and in patients with Cardiac Arrest". He has lectured on this topic and trained phyysicians all over the world. He also developed the technique of "Minimally Invasive Angioplasty". This technique reduces acute complications as well as restenosis. He was a leader in the evolution of the 'slow pass' techniques, developed to prevent complications during rotational atherectomy.

Having performed over 11,000 International Procedures, Dr. Shawl has been an innovator in working with the high risk patient, Dr. Shawl was the first interventional cardiologist to use the Eclipse Holmium Laser for Percutaneous Transluminal Myocardial Revascularization with Transesophageal Echocardiography guidance in the investigational treatment of end-stage atherosclerotic heart disease. Currently in pursuit of stroke prevention, Dr. Shawl has been a pioneer in perfecting the technique of carotid artery stenting. The results of this new endovascular therapy may challenge the accepted practice of surgical carotid endarterectomy.

Dr. Shawl has authored over 100 leading articles, abstracts, editorials and book chapters. He has also published a book entitled "Supported Complex and High RiskCoronary Angioplasty".

Interview

Q. What is "high risk angioplasty"?

Dr. Shawl: High-risk angioplasty means angioplasty in patients who have poor LV function alone or with other medical conditions that make them a high risk candidate for angioplasty or even bypass surgery. We mean people who have had previous multiple myocardial infarctions with multiple coronary stenoses. Or they have only one open artery which is also threatening to close. In these high risk patients, one cannot perform angioplasty or any other intervention because their heart will not tolerate the procedure. But with the support of the Percutaneous Cardiopulmonary Bypass Support (PCPS), the procedure can be performed very safely, even in patients in ventricular fibrillation.

Q. What kind of impact has PCPS had?

Dr. Shawl: The use of PCPS has helped many, many patients who otherwise would be crippled and require repeated hospital admissions. Some of them just waiting for a heart transplantation. Many of these patients can now undergo intervention with the PCPS system. On

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review of the cases and angiographic films, I say, “Listen, you are wait-listed a year or two to receive a new heart; meanwhile let's try this.” And of the last dozen cases that I did, over the last two years, four had such improvement that they did not require heart transplantation anymore because of improvement of LV fuction.

The other area where PCPS has played a major role is the sudden cardiac arrest in the cath lab. In these situations it is really a life saver.

Q. What alternative do patients have if they cannot undergo bypass or angioplasty?

Dr. Shawl: There are many patients who because of small size vessels or diffuse disease are not good candidates for percutaneous interventions or bypass surgery. These patients become severely limited because of ncapacitating angina. Percutaneous Trnsluminal Myocardial Revascularization (PTMR) can provide them with symptomatic relief of angina. In some animals, like crocodiles and alligators, the blood flow to the heart muscle is directly from the LV chamber via small channels. Based on this knowledge, Dr. Mirhoseini created channels in human hearts using laser energy. Over he last few years other surgeons have created similar aser channels directly into the heart muscle with bjectively evident beneficial effects.

However the surgical method is more invasive and is ssociated with 10-19% mortality. Now, using catheter-based technology, we are able to create channels from nside the chamber of the heart into the LV muscles. I performed the first few cases in humans last year in India, without any complications. We are presently doing PTMR in the U.S. with FDA IDE approval and have one a number of cases with great success and promising esults. I recently presented the results of these early xperiences at the ACC meeting in Atlanta. At six months 9 out of 12 patients showed objective mprovement.

Q: PTMR is still not approved in the U.S.?

Dr. Shawl: No, it's still investigational and is being tudied in a randomized fashion as per FDA approval. We are already in phase II period of the study and 90 cases have been done. Any patient who is not a candidate or bypass surgery or percutaneous interventions is ligible for this laser revascularization.

Q: Can you briefly describe carotid stenting?

Dr. Shawl: Basically it involves the same technique as or coronary angioplasty. Initially we dilate the lesion with balloon angioplasty and then palce a stent across the blockage. The whole procedure takes only half an our to 45minutes. And the risks are considerably less than carotid surgery even though carotid stenting is just evolving. I am sure that with further refinement in equipment and technique the risk will be even less.

Q. I know there is a lot of controversy about carotid stenting. How do you answer these concerns?

Dr. Shawl: Well, you know, it is the same as when we started doing coronary angioplasties in the late 70's and early 80's. The concerns were very similar all across the county. Even my surgeons at Walter Reed Army Medical Center, wared me, “Fayaz, don't do itn. It is not going to work and the Army will get a bad name.” That was then, in 1980. Look at it now, 20 years later, it is the treatment of choice. So it's the same with carotid intervention. Presently there is a lot of skepticism and reservations about this procedure, but having done more than 140 cases in the last two years, I feel it is much safer and far superior to the other methods of treatment which are currently available. I predict that in the next 5 to 6 years this will be the procedure of choice for carotid artery stenosis. We are in the process of arranging a randomized trial.

Q: What other areas do you see things moving in?

Dr. Shawl: I think an interventional cardiologist will be transformed into what I call a “vascular therapist”. He or she will approach evry vessel in the human body, from head to toe, particularly in view of the great availability of stents.

I also think adjunctive local injection of vascular growth factor shows great promise for many patients who would not be candidates for any form of revascularization. I am also excited about radiation therapy, particularly “beta”, which may further reduce the restenosis rate.

Q: Can you describe the technique of “minimally traumatic angioplasty”?

Dr. Shawl: One of the biggest problems and a persistent thorn in the side of the interventional cardiologist is the phenomenon of ‘restenosis’. Richard Myler has shown that the more the trauma to the artery durig angioplasty, the more the healing response, and the more the chances for restenosis. In the same context, I think the lesser the trauma, the lesser the haling response and the lesser chance of restenosis. I therefore described a technique of “minimally invasive angioplasty”, in which the lowest possible inflation pressure is used to dilate the vessel. If high pressures are needed, first an undersized balloon size is used, followed by a larger balloon. I think that if you can achieve “stent-like” results with balloon angioplasty, then the outcome is no different than stents. And this can be achieved in 30 to 40% of the cases, if balloon angioplasty is performed carefully. So I am not in favor of the prevailing 'stent-mania'.

Q: How can a physician tell whether or not to stent?
Dr. Shawl: Well, if the vessel is small, for example, less than 2.5mm in size, I would not stent it. In cases of non-ostial right coronary artery or circumflex artery lesions, if the balloon results are good angiographically, than I would not consider stenting it.

Q: If the result looks good anngiographically, then leave it alone?
Dr. Shawl: Yes. Especially in the circumflex and right coronary artery. But if it's a proximal LAD, a vein graft or aorta-ostial, there I would not waste time and I would proceed directly with stenting. I use stents in about 50% of cases, as opposed to others, who use it about 80%of the time.I think you cannot stent every lesion. Incases like bifurcating lesions,long lesios, small vessels, and where there is diffuse disease, stenting actually is associated with higher restenosis rates.

Q: So those are not good cases for stenting?
Dr. Shawl: Right. In bifurcating lelsions, I think rotational atherectomy is far superior and is associated with lesser resteosis. And in diffuse disease I think, along with balloon angioplasty,there is a role for stenting , but stenting only the area which is critical to start with and which does not look good angiographically. This I call "focal stenting". The restenosis with this technique is lower than using a long stent.

Q: You wouldn't put like 5 stents in a row.....
Dr. Shawl: No, no. That is horrible. They all come back.

Q: Do you find that it also compromises future procedures?
Dr. Shawl: Oh, absolutely. It makes future interventions very difficult. I am from Gurentzing's school of thought. I believe, "Do what is best for the patient". That is very improtant to me and I want others to learn likewise. That is the one reason I keep up with the tradition to Andreas Gruentzig, by teaching through demonstration courses both here and abroad. I must admit to you that over the past few years my frustration has been how may interventionalists are very keen to do quickly every form of intervention. I think that is bad. It really takes many many years to develop skill to do what I and others can do. They have to go through the process of learning.

Q: Your 10th annual coruse is coming up in May. you show complete cases and not just the highlights. Why do you show everything, unlike other courses?
Dr. Shawl: I desire to teach from skin to skin. That's my approach. I think people who come to attend the course want to watch everything: the good, the bad and the ugly. I think that's how you learn. I think if you just show them the pre-lesion and the post-lesion, it's just li reading a book or CD-ROM. But live demonstratio really means demonstrating the entire procedure. I thin it is important to show how to make desirable wire tip select appropriate balloons, where to park and mos important how to avoid complications. Similarly in othe situations how to select and deploy a stent and how t easily perform rota-ablation without running into problems.

Q: A final question: tell us what is a "hybrid procedure?
Dr. Shawl: I call it the "integrated minimally invasiv approach" or "hybrid procedure". You know, I alway say, "If bypass surgery were perfect, I would send ever patient of mine to surgery." But obviously it's not. T only advantage of conventional bypass surgery excellent outcome with arterial conduits like LIM RIMA, radial or gastroepiploic vessels. We can use the conduits by minimally invasive (MIDCAB) surgery. see no indication for conventional bypass or use of v grafts in the 21st century. In patients with multiple ves disease, instead of conventional CABG, we will u combined MIDCAB and percutaneous intervention the last 30 cases or so here at Adventist, we've do MIDCAB first, and then percutaneous interventions the remainig vessel the next day. And in a few we our new operating room/ cath lab will be opened, wh MIDCAB and percutaneous interventions can performed at the same sitting. This will be unique a as far as I know, the first lab to perform bypass a interventions at the same place on the same day.I We a very excited about it and hope that it will be a model f the rest of the country and the world.

Q: Are you going to be demonstrating a hybr procedure at your live demonstration course in Ma
Dr. Shawl: Of course, we will be doing li demonstrations of hybrid cases as well.

THE EDITOR WRITES

Dr. Fayaz A. Shawl has been my class fellow and best fri during our MBBS course at Govt. Medical College Srinagar. Dr. Sh was an active student and would take part in cultrual activites of college. He always had a smile on his face. He was first posted Assistant Surgeon in the Rajouri district of the State of J&K and th decided to go for higher studies abroad.

Since then he has made a place for himself amongst the Cardiologists of the world. He has trained many doctors of Indi Angioplasty. Besides coming as visiting Professor to rep institutions Dr. Shawl has delivered guest lectures in conferences over the world. I had an opportunity to observe him doing angiopl in Washington in 1986.

Dr Shawl has contributed a lot to the progress of our Journal - Practitioner. I am thankful to him.

Prof. G.M. M
Chief E

IN TO THE MILLENNIUM

The entry in to the Millennium heralds the Seventh year of publication of JK-Practitioner. The issue which you have just browsed through is the twenty secondth. The quarterly journal has been regularly coming out since the first issue was published in 1994. The hazards, the difficulties, the pressures and at times the frustrations of publishing a specialist journal from this place are many. As the editor-in-chief has already mentioned in his letter, the committed editorial and the advisory team has made the task less daunting and more enjoyable.

The journal has become a high quality forum for presentation of medical research, especially from the J&K State. The majority of the articles in the journal are from the medical institutes of the state - a purpose fulfilled, but we are expanding and the scope of the journal is widening. Articles from prestigious institutions of the country are being submitted to the journal and the number is increasing. With the flow of articles from abroad constant since its inception the journal hopes to maintain the international image with a distinct "geographical input"

Consistency in style, format content and policy takes some time. It has been established here earlier than expected. Yes, we have a policy of what goes to print. It is simple. All articles submitted to the journal are send to the reviewer (two, at times). The authors may not always agree with the referee and their displeasure is often expressed in writing or openly in person- an occupational hazard for every editor - perhaps.

With the importance of "Research Publications" for career promotion evident, the pressure on 'time' is increasing (other problem for the editor). This being a quarterly journal with "Original Articles and Case Reports" forming the core of the presentation, still only about 40 - 50 originals articles and 20 - 30 case reports will find way in to print every year. Besides the reviewer, the modifications/ the queries about the articles will take its time (postal services have never been a strong point of the administration). It may be 4 - 6 months before an article accepted for publication will actually be printed.

This gets us to the third problem-The Finances. Publishing a Journal, costs. It does not come free and the costs are rising. Usual sources of income for the journal are revenue from advertisements and personal subscriptions. The advertisements fetch a meagre sum for us. The stress will be on personal subscriptions. I earnestly hope, authors who receive acceptance letter for their articles will not hesitate to clear the dues in time.

As the journal strides in to the new millennium, we at JK-Practitioner will strive to make it better with every issue and as the journal establishes itself the rejections are bound to increase (at present 10 - 15% articles are rejected by the referees), the waiting period for accepted articles expected to prolong and the subscriptions and printing costs no doubt will escalate. I hope you will bear with us.

Wishing you a happy and prosperous new millennium.

Dr. Z.A. Khatib
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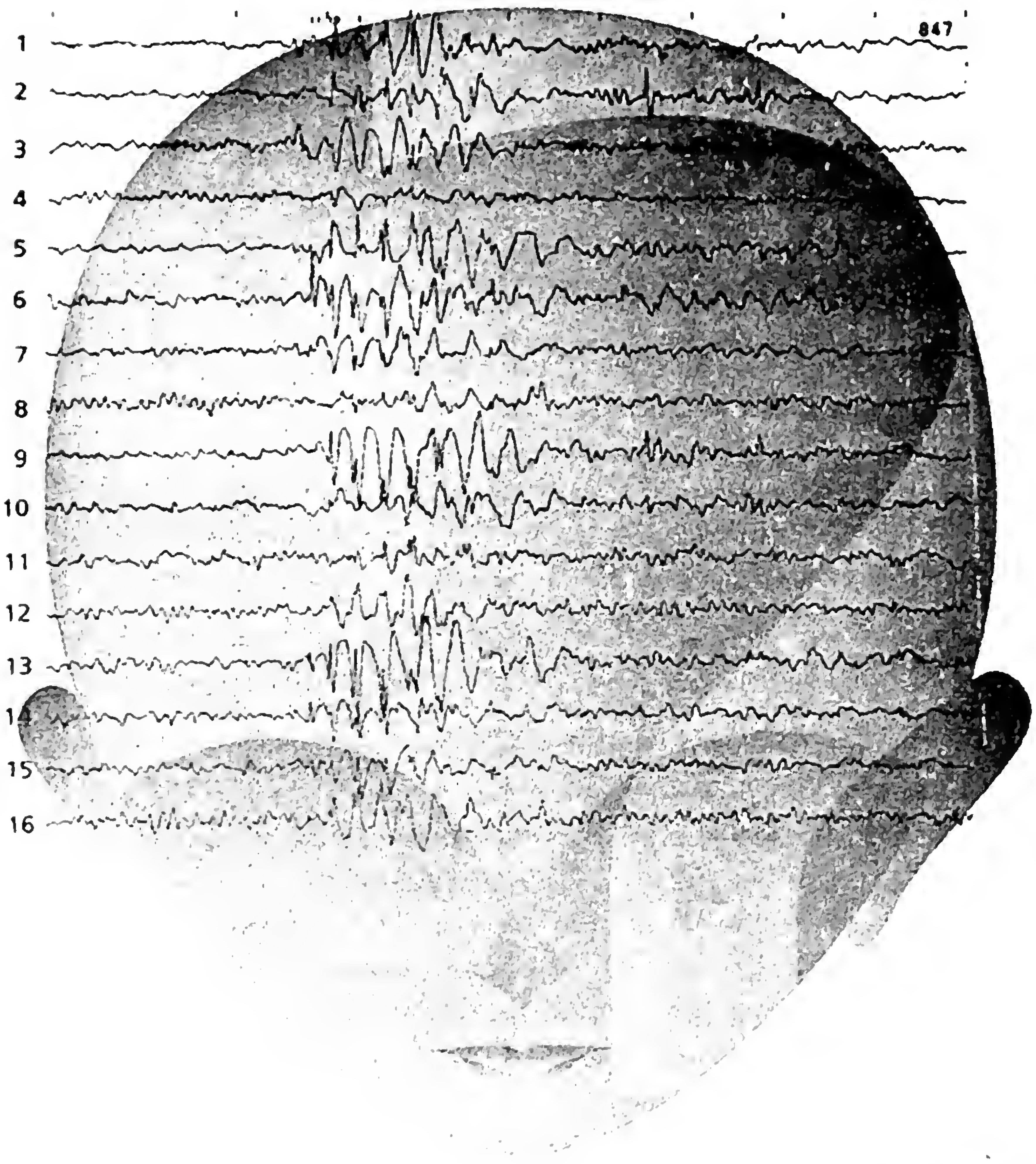
Inadequate seizure control
with a single drug...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ERRATA

II. Overseas Diary : **M. A. Mir : Post Graduate training for overseas doctors in the United Kingdom. JK-Practitioner 1999;6(4): 330-332.**
The above article was authored by Dr. Ayoub Mirza and not by Dr. M. A. Mir as indicated. The error is regretted. A summary of Dr. Ayoub Mirza's CV who authored the above article is given below.

Name : **Dr. M Ayoub Mirza**

DOB : 03-04-69

Dr. Ayoub Mirza graduated from Kashmir University in October 1994. After completing 1 year of Housejob (Internship) he worked for 6 months as a Senior House Officer in the Department of Surgery in SMHS Hospital. In June 1996 he came to UK for postgraduate training in Medicine. He did Clinical Observorship for 6 months in University Hospital of Wales in the Department of General Medicine. During this time he passed the PLAB Examination and he soon joined a 2 year programme of Basic Specialist Training in The Department of Medicine in University Hospital of Wales. During this training programme he passed the MRCP examination and gained the Membership of Royal College of Physicians of UK and full registration with the General Medical Council.

Dr. Mirza is currently working as a Clinical Fellow in the Department of Cardiology in Princess of Wales Hospital located in South Wales.

His aim is to get trained as a Specialist Cardiologist.

III. Case Report : **Ladakhi G. M. et al. : Pseudothalidomide Syndrome in Association with Intrauterine Infection. JK-Practitioner 1999;6(4): 316**
The following two photographs are to be included in the article

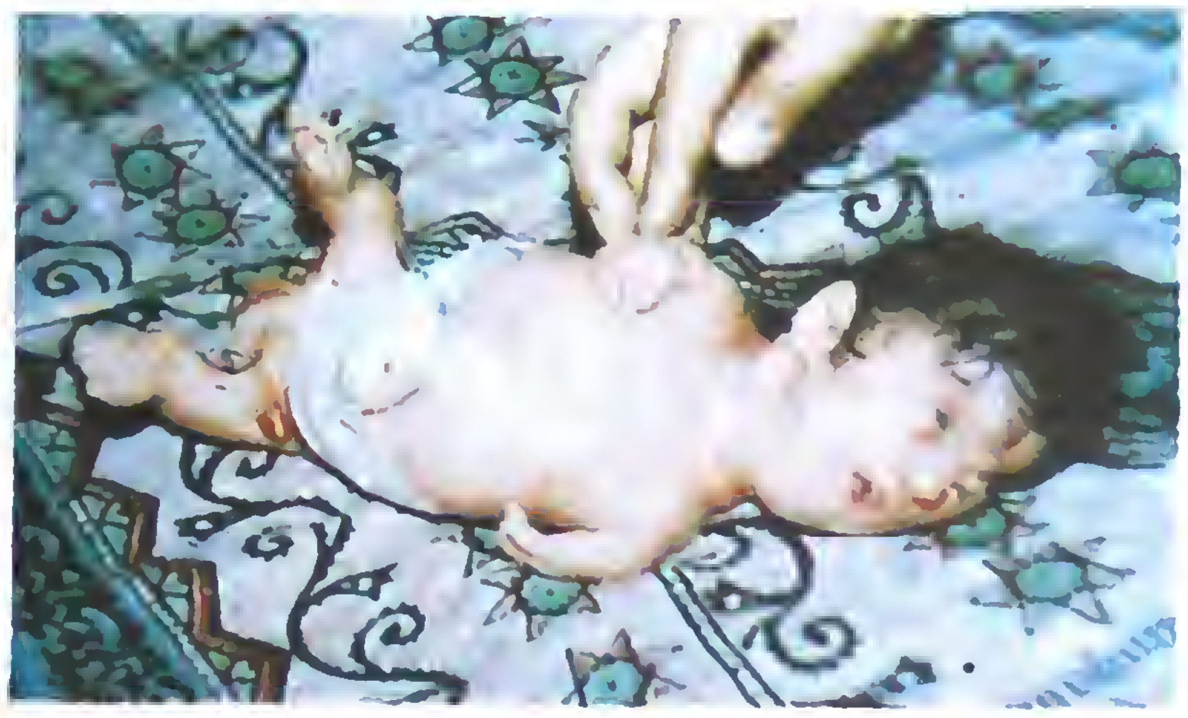

Fig-I
Showing the newborn with features of Pseudothalidomide Syndrome

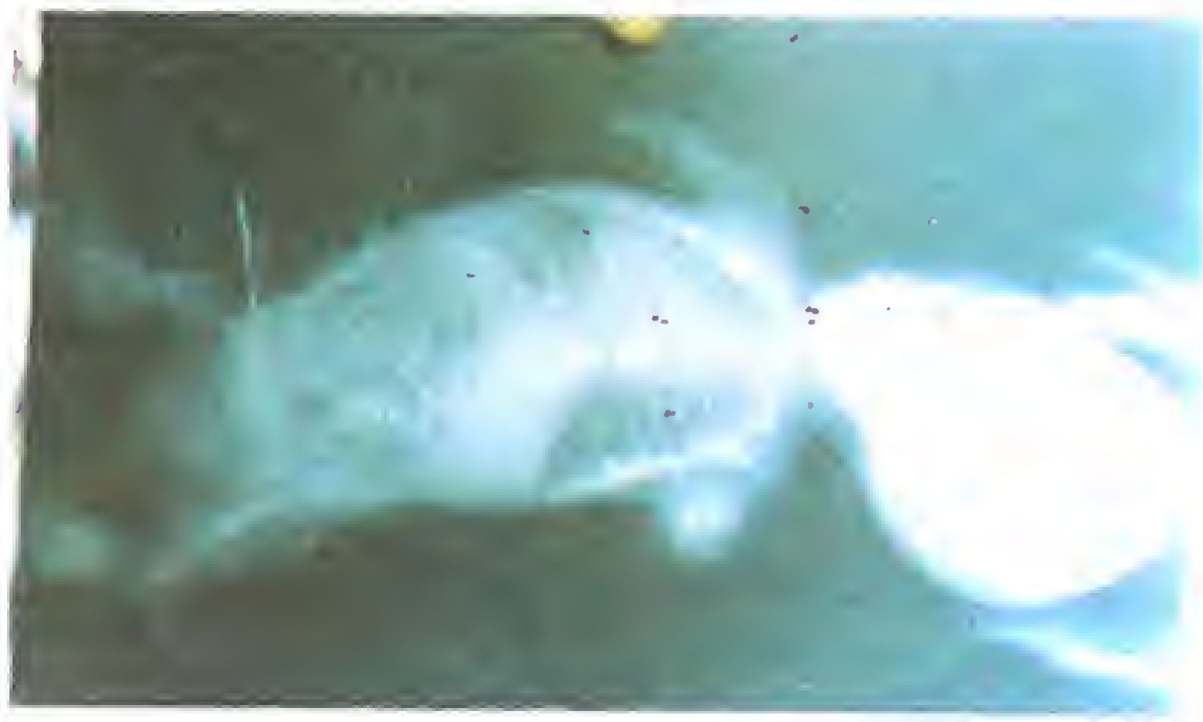

Fig-II
Showing Radiological features of the same

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EMERGING TRENDS IN THE MANAGEMENT OF UNSTABLE ANGINA

Unstable angina undoubtedlly is a critical phase in the natural history of coronary artery disease. The risk of acute myocardial infarction or death being high: upto 5% during hospitalization, 20% within 3 days and 25% in 6 months[1].

Risk assessment in patients with acute chest pain is frequently a difficult and time consuming process. The traditional approach is based on clinical symptoms, electrocardiographic findings and measurements of serum creatine kinase level. This approach has its share of limitations: too many patients are needlessly hospitalised and upto 5% patients are mistakenly discharged with infarction. Over the last decade several studies have documeted that troponin-T and troponin-I are independent markers which best predict the acute outcome of patients with unstable angina[2-7]. Approximately 30% of patients presenting with unstable angina have elevated serum troponin levels in the presence of no demonstrable rise in serum creatine kinase-MB fraction levels. The clinical characteristics and outcomes are being carefully defined in radomised and registry studies and the clinician has now access to multiple treatment options. In addition to cyclo-oxygenase inhibition with aspirin a number of other antiplatelet and antithrombotic approaches are available viz: inhibitors of ADP - induced platelet aggregation (ticlopidine and clopidogrel), glycoprotein IIb/IIIa receptor inhibitors (abciximab, tirofiban and eptifibatide) and direct or indirect thrombin inhibitors (heparin, low molecular weight heparins and hirudin). Each treatment option may be combined with a selective or non selective revascularization approach.

Release of troponins indicates the presence of minor myocardial injury which is most likely caused by downstream embolization of thrombus from a ruptured plaque of a large epicardial artery[8,9]. Troponins may therefore be a surrogate marker for active thrombus formation. Accordingly it can be postulated that potent antiplatelet durgs or anti—thrombins should be particularly effective in patients with elevated troponin levels. First evidence to support this concept stems from FRISC trial which showed superior benefit of low molecular weight heparin, dalteparin in patients with elevated troponin-T at 42 days follow up[10]. In unstable angina patients in addition to aspirin treatment with various low molecular weight heparins viz.: enoxaparin[11], dalteparin[12], nadroparin[13] given subcutaneously twice daily for 3-7 days, have been shown to be atleast as effective as heparin infusion. Prolonged low molecular weight heparin treatment with dalteparin twice daily can be given in a weight and gender adjusted dose as an outpatient treatment which is beneficial in patients waiting for invasive procedures[14]. Invasive therapy is required in a significant number of patients with unstable angina with elevated troponin levels and has been shown to reduce several composite end points as compared to non-invasive arm. Death/non fatal MI (9.4% vs 12.1, p=0.031), non fatal MI (7.8% vs 10.1%, p=0.045), death (1.9% vs 2.9%, p=0.01), recurrence of angina (22% vs 39%, p<0.001)[14]. Treatment with low molecular weight heparin is associated with a low but increased risk of bleeding which increases with the duration of treatment.

Hirudin is a more effective inhibitor of clot bound thrombin than anti-thrombin III dependent inhibitors like heparin[15]. From the GUSTO (Global use of strategies to open occluded coronary arteries) IIa, TIMI 9a annd HIT (High density lipoprotein intervention trial) studies, higher doses of hirudin without adjustment of activated partial thromboplastin time resulted in major bleeding, including cerebral bleeding. In the GUSTO IIb trial, using a lower dose of hirudin the frequency of death, myocardial infarction was approximately 20% lower in the hirudin arm at 7 days, but there was no significant difference at 30 days[16]. The OASIS-2 trial which included more than 10,000 patients showed a modest beneficial effect of hirudin in a medium dose range (bolus 0.4 mg/kg followed by 0.15 mg/kg/hour) for 72 hours (P=0.077) when compared against unfractionated heparin at 7 days. The benefit was maximum in the group of patients who had marked ischaemia or required inteventions and the treatment effects persisted for 6 months. There was however an excess of major bleeding in patients given hirudin (1.2% vs 0.7%) but no excess of strokes.

The totality of evidence based on a combined analysis of OASIS-I, OASIS-2, TIMI 9b and GUSTO IIb indicates 22% relative risk reduction in death or myocardial innfarction at 72 hours with a relative risk reduction of 0.83 at 7 days and 0.90 at 35 days[17] and is superior unfractionated heparin. We however lack direct comparison between hirudin and low molecular weight heparin which is the most widely used anti-thrombin in unstable angina.

The key role of plaque rupture or erosion followed by local thrombus activation has been recognised as the underlying pathophysiological mechanism in unstable angina and acute myocardial infarction[18]. Typically a grey platelet rich thrombus is the culprit in the syndrome of unstable angina[19]. Accordingly it is reasonable to assume that the new group of glycoprotein IIb/IIIa antagonists, the most potent antiplatelet compounds have been found to be effective in this scenario. However in large trials with the antibody abciximab or synthetic compounds like tirofiba, or eptifibatide the overall benefit has had a low statistical significance[20-22]. We therefore need a better understanding for the indications of use of these aggressive antiplatelet agents. CAPTURE (Chimeric 7E3 Antiplatelet Therapy in Unstable Angina Refractory to Standard Treatment) Study results when relooked at in the group of patients with raised troponin-T levels showed that the treatment benefit of abciximab relative to placebo in patients with elevated troponin T resulted in a relative risk reduction of 0.32 (odds ratio: 95%, CI: 0.14-0.62, p=0.002)[23]. The lower event rates were attributable to a reduction in the myocardial infarction rate. This post hoc analysis showed that treatment of 100 patients with elevated troponin T levels undergoing PTCA and treated with abciximab rather than standard treatment with heparin and aspirin only would prevent 15 cardiac events. These findings, seems to be of great importance because they may implicate a new therapeutic concept in the treatment of patients with unstable angina. These findings link the new diagnostic potential of troponins with the therapeutic advance of glycoprotein IIb/IIIa receptor antibody abciximab. The data also allow us for optimal patient selection since these agents are very expensive. Combinations of low molecular weight heparin with the new platelet inhibitors are presently under evaluation in several ongoing trials and might represent the next step in the development of treatment of unstable coronary artery disease which has the potential of being a break through.

The role of HMG CoA reductase inhibitors (statins) and inhibitors of the degradative enzymes which weaken the fibrous cap, making it more prone to rupture are currently being assessed in plaque stabilization. A study recently reported by the Cholesterol and Recurrent Events (CARE) investigators[24] showed that evidence of inflammation (increased levels of C-reactive protein and serum amyloid A) after myocardial infarction is associated with increased risk of coronary events and that treatment with pravastatin may decrease this risk, an observation consistent with a non-lipid effect of this statin.

There is also growing evidence that infectious agents such as chlamydia pneumoniae play a role in atherosclerosis. A preliminary report from the ROXIS study group[25] showed a significant reduction in ischaemic events at 30 days in unstable angina patients treated with the antibiotic, roxithromycin. The final report from the group[26] shows that the clinical benefit of preventing death and re-infarction is maitained for at least 6 months. If further studies which are underway are consistet with the ROXIS findings, antimicrobial chemotherapy or vaccination against infectious agents may be appropriate for some heart disease patients.

It is clear from the present data on management strategies of unstable angina that all patients with acute coronary syndrome do not require cardiac catheterization. However it is sensible to consider conservative and invasive treatment strategies as complimentary rather than competitive. There is a compelling evidence to favour the use of low molecular weight heparins in patients with acute coronary syndrome in addition to aspirin. It is now possible to identify a group who will benefit from interventions. Such patients could be protected further by adminnistering glycoprotein IIb/IIIa inhibitors.

Have we reached the limits in term of improving outcome with the currently available therapetic regimens? The answer is still debatable, however it is very clear that all patients with unstable angina need to be treated aggressively in order to neutralise the effects of vulerable disruptive atherosclerotic plaques. The management of cardiovascular risk factors in this regard especially the problem of dyslipidemia is critical.

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THE DECADE OF THE BONE AND JOINT 2000 - 2010

Professor L. Lidgre, M.D., Ph.D, Chairman of the Department of Orthopaedic Surgery began the Decade initiative at Lund University in Sweden. He wanted to determine whether support could be obtained for musculoskeletal disorders by having the years 2000-2010 designated in a way similar to the Decade of the Brain 1990-2000 proclaimed by President Bush in 1990. The Brain campaign generated widespread publicity ad went some way towards improving awareness in that regard.

Professor Lidgrenn was given a planning grant from the Swedish Medical Research Council, and aided by Lund University so that, in 1998, he was able to organize a consensus meeting which was also co-sponsored by the World Health Organization. The meeting was attended by delegates representing more than fifty professional and patient organizations, as well as numerous scientific journal representatives. The delegates agreed to launch the Bone and Joint Decade at the conclusion of the meeting. In November 1999, the Bone and Joint Decade was welcomed and supported by the United Nations in an announcement made in conjunction with the World Health Organization endorsement. It officially started on January 13 of this year.

The reason for the initiative can be understood in the following way: Musculoskeletal problems are the most common causes of long-term pain and physical disability affecting hundreds of millions of people throughout the world. In particular, joint diseases are responsible for at least fifty per cent of all chronic conditions in persons who are aged or over. Fractures are increasingly being related to osteoporosis.

There are also other varied problems. For instance, back pain is the second most common cause of time beig taken off work (sick leave). Further, more and more, the injuries suffered by populatios particularly as a result of traffic injuries or war are producing a commesurate increase in the need for both preventative ad restorative procedures.

The basic goals of the Decade are:

1. Raisig awareess of the growing burden of musculoskeletal disorders on society.
2. Empowering patients too participate in their own care
3. Promoting cost-effective prevention and treatment.
4. Advancing the understanding of musculoskeletal disorders through research to improve methods of prevention and treatment.

A Steerig Group composed of representatives of various geographical regions ad disciplines is co-ordinatig the campaign. An initial focus will be the health-needs assessment for musculoskeletal disorders which will aid in the development of strategies that are relevant to particular geographical, social and economic bearing of those suffering in a given setting.

Already, in Brazil, various Decade-related campaigns have been conducted. For example: the procurement of a national minute of silence last year during Trauma Week (Nov 4—11) to honour victims of violence and trauma: Safe Home 99, which focused on elderly individuals; and a nationwide car accident prevention program emphasizing the use of seat belts which has also helped in creating improved driving laws.

In the last analysis, the Decade must be seen as a framework for local action. In our part of the world Trauma is neglected or seen late. Childrens' deformities, bone ad joint sepsis includig tuberculosis, are the major preoccupations.Malnutrition and related bone problems are common. Since the Decade campaign is global, it will include initiatives in any geographical location and will try to support activities in developing countries. The Decade should be endorsed by the government of Jammu and Kashmir State followed by professionals, patient organizations, scientific journals and relevant research bodies in consultation with all other stakeholders from all countries and regions.

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CHILDHOOD TUBERCULOSIS (PART-II) (DIAGNOSIS AND MANAGEMENT)

M. Mubarik M.D.; Basharat Nahi M.D.; G.M. Ladakhi M.D.; A.S. Sethi M.D.

The discovery of tubercle bacillus by Robert Koch in 1882 was the starting point for many further advances including diagnostic and therapeutic. A multitude of investigative approaches and treatment regimens have been devised over a period of time. However, careful consideration and investigation will be required to determine if and how the results of new diagnostic tests should influence the definitions and treatment of tuberculosis in children[1].

Investigations:

(i) Intradermal skin tests:

a) Mantoux Test: Mantoux test is the most accurate definitive and reliable skin test. The test consists of given ITU of PPD (0.00002mgs PPD-s) intradermally by using a 26 gauge needle and tuberculin syringe. The induration is measured after 48-72 hours. If a patient is to show up for reading, it is acceptable to read the result for upto 1 week after testing, if the result is positive. Any patient who does not return to have his skin test read at 48-72 hours and who has a negative result 4-7 days should be retested. Mantoux should not be repeated more than twice in a month[2].

Internationally Proposed Interpretation[3,4]

	Risk factors	Size of Induration	Interpretation
1.	Not known	≥ 15 mm	Positive
2.	Moderaterisk (a)	≥ 10 mm	Positive
3.	High risk (b)	≥ 5 mm	Positive
4.	BCG Immunization (c)	≥ 15 mm	Positive

Interpretationof risk factors

a. Childrenborn in high prevalence area-Asia Africa; children who are I/V drug users; children living in shelters for homeless or Institutions; children who have malnutrition, diabetes mallitus. Hodgkin's lymphoma, lenkemia.

b. Children with radiographic evidence of tuberculosis, who were in recent contact of someone with tuberculosis who is smear positive or children who have cellular immune deficiency as HIV.

c. If not in moderate or high risk catagories.
In India cut off limit for Mantoux is taken as ≥ 10 mm, being a hig prevalence area.

Indications for Tuberculin Testing (As proposed by American Academy of Paediatrics)

a.	Immediate Testing.	1.	Suspected TB on X-ray or clinical findings.
		2.	Contacts of confirmed or sspected cases.
		3.	Immigrants from endemic areas.
b.	Annual Testing:	1.	Children with HIV
c.	2-3 Yearly testing:	1.	Children exposed to HIV patients or drug abusers.
d.	Testing at ages 4-6 and 11-16 years	1.	Children without high risk factors, residing in high prevelance areas.
		2.	Children whose parents immigrated from high TB prevalence regions.
	False .Positive Reactions:	1.	Repeated skin testing with PPD or old tuberculin.
		2.	Non-tuberculos mycobacterial infection.
		3.	Prior BCG Vaccination can cause transient reactivity to a subsequent tuberculin skin test, but the association is weaker than commonly recognised. In many studies 80-90% of hildren who received BCG vaccination as infants, have a non-reactive tuberculin test by 5 years of age[4,5-7]. A study has, however, shown that BCG given at birth or to school age children causes a reactivity to tuberculin, which persists for 20-25 years[6].
	False Negative Reaction:	1.	Normally a period of 2-10 weeks is required for DTH response to develop after infection. Testing done during this period is negative.
		2.	Severe systemic tuberculosis. Anergy, Immunodeficiency, malnutritioin, infections as measles, mumps, rubella.
		3.	Improper dilution, bacterial contamination, exposre to heat or light or loss of potency of tuberculin.

b. BCG Tests: BCG when used as a diagnostic test has been found to be valid in many studies in confimity

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with our experience at our hospital[9]. Accelerated reaction to BCG is taken as an evidence of active infection. BCG test can be done without prior Mantoux or if Mantoux is negative and can infer a strong suspicion of tuberculous infection. The reading is taken on day 3 but can also be taken from 24-28 hours to 10 days[4,10].

Interpretation:

Time duration Positive BCG (Accelerted Reaction)[11]

48 - 72 hours	induration 5 - 9 mm	1 + (Mild)
48 - 72 hours	Induration 10 - 20 mm	2 + (Moderate)
48 - 72 hours	Induration 21 - 30	3+ (Severe)
5 - 8 days	Pustule formation	
10 - 15 days	Healing with scab formation	

1 + Positive reaction in non-vaccinated and malnourished children. 2 + and 3 + positive reaction in vaccinated children especially under 5 years.

Udhani et al, Desai 1972, Muller, 1982, found that BCG is positive in 90 - 100% of cases of tuberculosis inspite of presence of malnutrition, serious disease as miliary or meningitis and even during steroid therapy. A study conducted at our hospital during 1994-96 also vindicates the viewpoint of above authors. Table - (1) (Unpublished data).

Table-1 Mantoux and BCG induration sizes among children having tuberculosis (Study conducted at Govt. Hospital for children Sgr. 1994-96)

Age group	Cases %	Cases %	BCG + VE Mean Induration	Mantoux + VE Cases %	Mean Induration
2- yrs.	18	18	12.5mm	6	11.6
2-4 yrs.	22	22	12.0	14	10.6
4-6 yrs.	25	25	10.7	8	12.1
6-8 yrs.	15	15	10.4	4	10.5
8-10 yrs.	9	9	10.4	2	10.0
10-12 yrs	11	11	10.2	4	12.5
Total	100	100	11.0mm	38	11.2 mm

Note. Mx testwas +ve in 38 cases only & doubtful in 14.

BCG test was +ve in all 100 cases with 71% showing >10mm induration.

ii. **Mycobacterial detection and Isolation:** Depending on location of disease, examination of sputum, gastric aspirate,bronchial washings, lung tissue, lymphnode tissue, bone marrow, liver, blood, CSF may be undertaken.

Sputum analysis: is more useful in older children especially if endobronchial TB is present. Cought may be stimulated by aerosol solution of 10% saline[12]. WHO recommends at least 3 (not>6) morning samples. Saliva and nasopharyngeal secretions are not acceptable. Decontamination of specimens is done by Sodium hydroxide usually in combination with N-acetyl L cystine (NALC).

Gastric aspirate: It yields organisms in 18-71%, with higher yield in children with extensive pulmonary disease[7,13]. The gastric fluid is aspirated early in the morning as child awakens before the stomach empties itself of overnight accumulation of secretions, swallowed from respiratory tract. The stomach is then washed with 30 ml of water and the washings are added to aspirated material. If transport to laboratory is delayed. PH of material is neutralized with Soda bicarb till it is just pink with phenol red. The procedure is repeated on 3 consecutive days.

Fiberoptic bronchoscopy with bronchoalveolar lavage (BAL) and or biopsy has a high yield and is useful in patients who have difficult in producing sputum or whose initial sputum specimens are negative for AFB.

Body fluid specimens are analysed for differential cell count for glucose and protein content. Tissue biopsy (liver, lymphnode etc.) specimen should be sent to laboratory for culture as well as for histological examination[14].

Smears of CSF are positive in <10% cases, Pericardial and pleural fluids are culture positive in 40-86% and 23-67% of cases respectively[15].

Microscopy with Ziehl Neelson staining, the limit of detection is 5,000 - 10,000 bacteria per ml of sputum. Using Auramine O in place of carbol fuchsin dyes makes smear reading advantageous as yellow fluorscent bacilli are easier to detect and also smears are read in low power in fluorescent microscopy, so that larger areas are screened in less time.

Culture: Culture of specimens is more sensitive than direct smears, whereas 5000 - 10000 AFB per ml of sputum are detected by direct smear, only 10 AFB per ml can give a positive result with culture. Traditionally used solid media (Lowenstein Jensen, which is egg based and Middlbrook 7H 10 and 7H 11, which is agar based) require 6-8 weeks for colonies to appear and liquid medium (Dubos Oleic Albumin) that requires an incubation in 5-10% of CO_2, takes 3-8 weeks. Newer rapid diagnostic culture methods include:

a. **BACTEC System:** This uses a liquid Middbrook 7H12 medium containing Radiometric Palmitic acid labelled with ^{14}C. Growth of mycobacteria within the system is measured as a daily growth index that detects the production of $^{14}CO_2$ by the organisms. Advantages incluude rapid detection (5-7 days) increased sensitivity and species identification. Disadvantages include radioactivity, the disposal of which is problematic[16,17].

b. **Septichek:** This uses a biphasic medium in self contained CO_2 environment. It takes 3 weeks for incubation and advantages include non-radiometric nature, obviates CO_2 incubation requirement and simultaneous detection of M. tuberculosis, non tuberclous mycobacteria, other respiratory pathogens and even contaminants[17-19].

c. **Isolator tube** is a unique approach to recover mycobacteria from blood 10 ml of blood is collected in a tube with anticoagulant and saponin which lyses RBCs releasing any microbes within. After centrifugation, the sediment is inoculated into a variety of mycobacterial media.

d. **Mycobacterial Growth Indicator Tubes (MGIT):** It is non-radiometric brisk method wherein antibacterial and antifungal agents with growth supplements are added before inoculation. Positive cultures are detected usually because of metabolic depletion of O_2. The tube is examined under UV light and growth is indicated by orange fluorescent glow[18,19].

iii. **Immune Diagnosis: 1. Enzyme Linked immunosorbant Assay (ELISA):** has been developed to detect serum IgE antibodies to antigens of M. tuberculosis including PPG sonicate, antigen 5, 6 A60, 12,384D, P32 and lipoarabinomannan (LAM). The sensitivity varies from 45-95% and specificity from 90-100%[18-23]. Antigen 60 is one of the best known antigens used in TB ELISA method, having specificity and sensitivity of about 80%[23]. ELISA testing can be performed on blood, sputum, bronchial washings (BAL), pleural fluid and CSF for diagnosis of pulmonary and extrapulmonary TB. The disadvantage is false positive result after BCG vaccination and infection with atypical mycobacteria.

2. **Soluble antigen Fluorescent antibody test (SAFA).** Antibodies are detected by using soluble tubercular antigen absorbed on a cellulose acetate paper[24].
3. **Polymerase chain reaction (PCR):** Wherein a given sequence of DNA or RNA is amplified by using thermus aquaticus (TAQ) polymerase. Starting material may be as less as < 1AFB and amplified sequences are detected by gel electrophoresis. PCR takes <3 days for results[25].
4. **Ligase chain reaction (LCR)** is similar to PCR but here fragmented primers are amplified rather than the target site. This method can be easily automated.

iv. **Non-Specific Tests:** Certain non-specific markers like ESR, serum gloublins, carcino-embryonic antigen, LDH and lysozyme levels are increased in TB and have a very high false positive and false negative results.

Bromide Partition Test: is a non-specific test for early diagnosis of TBM. A loading dose of radioactive bromide is given and ratio of bromide in serum to CSF is determined. In TBM, the blood brain barrier to bromide is lost and more bromide appears in CSF. The ratio of serum to CSF bromide of <1.6 signifies TBM with sensitivity and specificity of 90%.

Adenosine Deaminase Activity (ADA): An enzyme which converts adenosine to inosine is increased in peritoneal, meningeal, pleural andpericardial TB. The specificity is 99.4% in TBM as reported by Bargava et al. The sensitivity and specificity is also high in differentiating TB ascites from other causes of ascites[24].

v. **Radiological Investigation:**

1. **Chest X-ray:** may demonstrate adenitis (hilar, paratracheal and subcarinal), parenchymal lesions, miliary mottling, pleural effusion, collapse etc. Caffey's four views (Postero anterior, lateral, apical lordotic and oblique) increase the possibility of (detecting lymphadenitis.
2. Bone X-rays show up lytic lesions.
3. USG abdoman.
4. **CT scan and MRI** for demonstration of tuberculomas in brain and tuberculous meningitis with developing hydrocephalus.

Diagnosis of Tuberculosis in Children:

The diagnosis of tuberculosis in children is different because.

1. Children can't cough out sputum. The sputum smear and culture are otherwise "gold standards" for diagnosing pulmonary TB in adults.
2. Tuberculin Test, often used gets positive about 3 months after infection during which time children, especially under 5 years of age, may develop meningeal or miliary TB.
3. Pulmonary TB in children, unlike in adults, is usually in the form of mediastinal lymphadenopathy often

without a primary parentchymal lesion. This lymphadenopathy is difficult to pick up with traditional AP and lateral views only and may be missed.

The diagnosis of TB in children is always presumptive as bacteriological confirmation is not possible

Various scoring systems have been devised to improve diagnosis of childhood TB, with a score beyond a particular threshold indicating increasing likelihood of TB.

i. WHO Provisional Guidliness for Diagnosis of TB in children:[26]

1. **Suspected TB:** Any child a/ with history of contact with a confirmed case of pulmonary TB. b/ not gaining normal health after measles or whooping cough. c/ loss of weight, cough and wheeze not responding to antibiotic therapy for respiratory disease. d/ painless swelling in superficial group of lymphnodes.
2. **Probable TB:** A suspect case with any of the following a/ positive induration of Mantoux. b/ suggestive radiological findings. c/ suggestive histological findings of biopsy material. d/ faourable response to ATT.
3. **Confirmed Tuberculosis:** a/ Detection of tubercle bacilli by microscopy or culture from seretions. b/ Identification of tubercle bacilli as Mycobacterium tuberculosis by culture characteristics.

ii. Udanis Simple Scoring Technique[27]

Criteria	Score
a. History of symptoms like irregular fever, cough particularly pertussoid and /or persistant bronchitis, loss of weight or poor appetite over a period of 2 wks or more, with no evident cause like fever, headache, vomiting, meningeal signs etc.	3
b. In contact presently or in recent past with a sputum positive tuberculous adult.	3
c. Positive tuberculin test ($\geq$ 10 mm even in BCG vaccinated children).	3
d. Negative tuberculin but positive BCG test in high risk population particularly in children <5 years.	3
e. Positive chest x-ray finding	3
f. Prolonged illness of 6-8 weeks after an attack of measles or pertussis.	3

Interpretation:

Score < 3 - Probably negative
- TB is unlikely
However high risk subjects may require chemoprophylaxis.
Score 3 - 4 - Probably possitive, TB is likely or suspected and needs further evaluation and treatment or chemoprevention.
Score 5 - 6 - Probably TB and needs chemotherapy
Score 7 & above- Established tuberculous disease.

iii. Kenneth Jones Scoring[28]

Criteria	Score
a. 1/ Demonstrable bacilli, 2/TB granuloma 3/ positive Mantoux atet (>10m)	+ 3 (each)
b. 1/ Suggestive x-ray chest, 2/ suggestive physical findings. 3/ doubtful Mantoux test (5-9 mm), 4/ Recent Mantoux conversion, 5/ contact with sputum positive case.	+ 2 (each)
c. 1/ Non-specific x-ray changes, 2/ compatable physical findings, 3/ history of contact. 4/ non-specific granuloma. 5/ age under 2 years	+ 1 (each)
d. BCG vaccination in previous 2 years	-1

Interpretation Scope of $\geq$ 7 usually suggests tuberculous disease.

Management of childhood Tuberculosis:[29]

Indian Academy of Pediatrics (IAP) working group in January 1997 standardized certain recommendations to ensure ideal treatment for TB or most of the clinical situations met within routine practice. Tuberculosis has been classified into 5 groups based on clinical types to optimize treatment protocol.

The drugs used are - Ethambutol (E), Isoniazid (H), Rifampcin (R), Streptomycin (S),Pyrizinamide (Z). (Table-2).

Group-I Preventive Therapy): 6- HR (i.e. 6 months Isoniazid and Rifampcin).

Indications:

1. Asymptomatic Mantoux positive < 3 yrs age.
2. Asymptomatic Mantoux Positive <5 yrs age with Grade III/IV PEM
3. Mantoux positive - Recent converter / no signs (Recent converter is one who shows an increase in induration of $\geq$ 6 mm within 2 years period).
4. Children < 3 years age with history of positive contact.

5. Children < 5 years with grade III and IV PEM with history of positive contact.

Group-II: 2-HRZ / 4-HR
Indications:
1. Primary complex (lungs)
2. Symptomatic Mantoux positive < 3 years age - wihout localization.
3. Symptomatic Mantoux Positive <5 years age with grade III or IV PEM without localization..
4. Isloated lymphadenitis.
5. Pleural effusion.

Group III: 2-HRZE /4-HR
Indications:
1. Progressive pulmonary disease.
2. Tubercular lymphadenitis (Multiple) - in case of nonresolution of lesion extend continuation phase by 3 months.

Group IV: 2-HRZE / 7-HR
Indications:
1. Miliary / Disseminated disease
2. Cavitatory disease / Bronchopneumonia
3. Osteoarticular disease
4. Abdominal, pericardial, genitourinary disease.

Group V: 2-HRZE / IO-HRE
Indication - Neurotuberculosis

Table -2: Recommended Dosage of drugs (ATT)

Drug	Daily Therapy (mgs/Kg)	Intermittent Therapy (mgs/Kg)
INH	5*	15
Rifampcin	10	15
PZA	25	30
Ehtambutol	20	30
Streptomycin	20	30
Prednısolone	1	30

Never <5 mgs/Kg - to be rounded up to the closest higher dose

Comments
1. All drugs mentioned above are to be given ina single daily doseon an empty stomach.
2. The drugs are safe in recommended dosage schedule
3. Vitamin B_6 is not necessary in children on INH
4. Hepatotoxicity may be seen in vulnerable patients (manutrition, disseminated disease)

Prednisolone Indications:
1. Neurotuberculosis
2. Miliary TB
3. TB involving serous layers
4. Endo bronchial TB/segmented
5. Genitourinary TB/ Sinus formation lesions

Usual dose is 1-2mgs/Kg/day for 4-8 weeks, whereas in Neurotuberculosis it is 8-12 weeks.

Baby born to mother with TB (Diagnosed in 3rd trimester or during delivery) - Breast feeding is to be continued, unless multiple drug resistance (MDR) is suspected. BCG to be given at birth. If x-ray is normal, 6-HR is given. If x-ray abnormal - 2-HRZ / 7-HR is given.In case of congenital tuberculosis 2HRZ / 7HR is given.

Hepatotoxicity: Clinical symptoms, hepatomegaly with Jaundice merit laboratory tests and temporary stoppage of hepatotoxic drugs and suggested line of action is to stop INH, RMP and PZA and start streptomycin (SM) and EMB. When SGPT returns to normal (2-4 weeks), restart INH at 5 mgs / kg dose. Restart RMP after 1 week. Stop SM and EMB and restart PZA after 1 week (if stopage occured in intensive phase of therapy).

Defaulters: Treatment discontinued for > 1 week.
2. lost to treatment and period of default > 1 week.

Suggested line of Action:
1. Defaulter (1 week to 1 month) continue same phase of treatment for additional one month.
2. Lost to treatment - restart full treatment.

Drug resistance: If a patient on prescribed treatment dose not respond, check drug compliance, confirm diagnosis and assess for probable adult contact with MDR TB. Arrange for bacteriological study, if possible.

In case of suspected drug resistance in absence of bacteriological proof, give 2-SRKZE / 1-HRE. However,in case of proved drug resistance the following regimen is prescribed.

	Drug Resislance to		
Patient Group	1NH	RMP	Mltidrug (MDR)
HIV Negative	12 (RZE)	18-24 (HZE)	3 Sensitive drugs for 2 years after culture negative.
HIV Positve	18(RZE) or 12 months after culture negative	18-24 (HZE) months or 12 months after culture negative.	3 sensitivedrugs for 2 years after culture is negative

Relapse: defined as reappearance of signs and symptoms of tubercular disease within 2 years of cure after completion of specified therapy.

Suggested line of Action: The patient should be taken as suspected drug resistance in absence of bacteriological proof and treatment started accordingly.

Contact: defined as any child who lives in a household with an adult taking ATT or has taken ATT in past 2 years.

Indications for Preventive therapy for contact:

Age < 3 years, < 5 years with PEM (grade III and IV) and adolescents. Close surviellance is necessaryfor 5-12 yearsold contacts. Suggestive preventive therapy for contacts - 6-HR.

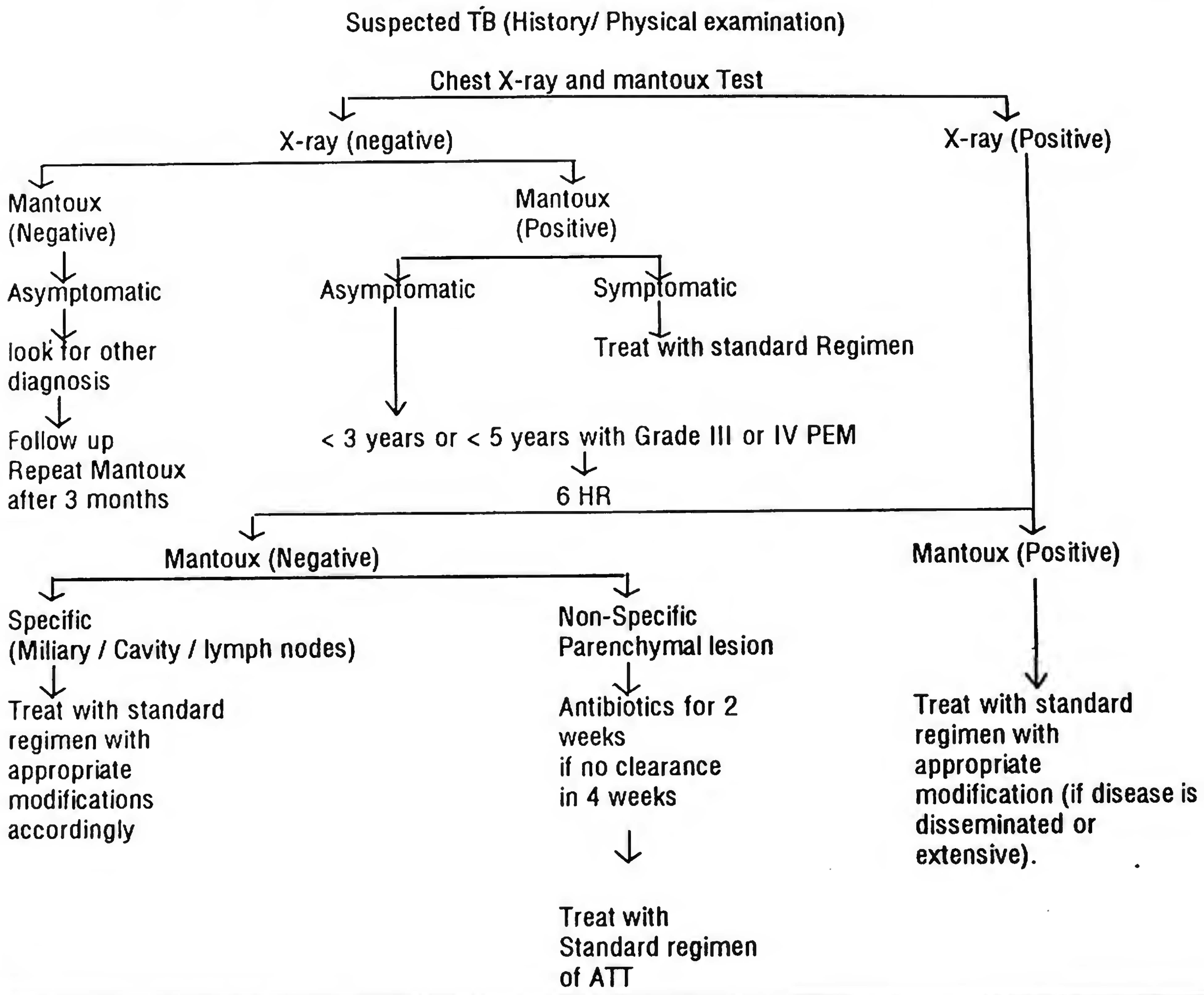
BCG Adenitis: No treatment is given if lymphnode size is < 1.5 cm. If, the lymphnode is increasing in size or is fluctuant, treatment is excision or 3-6 H. If sinus formation has occured, excision is indicated.

Role of BCG Vaccination in Prevention of Childhood Tuberculosis

Studies have shown that BCG gives a range of protection which varies from 0 - 80% in different parts of world. Although full explanation for varying degree of protection has yet to be found,[31,32] one suggestion is that prior exposure to some non-tuberculous mycobacterial (e.g. M vaccae, M non chromogenicum) may have conferred partial immunity on the population and thus masked the potential benefit of BCG vaccination[33]. There is also evidence that exposure to other species (e.g.M. Kansasi) have antagonist action against BCG[34]. This may be one reason why BCG was not found to be protective in South Indian trial[35].

There is a large body of evidence that supports the conclusion that BCG does gie appreciable degree of protection against childhood tuberculosis as it decreases riskof TBM and miliary TB by 52 - 100%, although pulmonary tuberculosis is decreased by a veryless margin

Fig.1: Flow Chart for management of Childhod Tuberculosis


Suspected TB (History/ Physical examination)
Chest X-ray and mantoux Test
X-ray (negative)
X-ray (Positive)
Mantoux (Negative)
Mantoux (Positive)
Asymptomatic
look for other diagnosis
Follow up Repeat Mantoux after 3 months
Asymptomatic
Symptomatic
Treat with standard Regimen
< 3 years or < 5 years with Grade III or IV PEM
6 HR
Mantoux (Negative)
Mantoux (Positive)
Specific (Miliary / Cavity / lymph nodes)
Treat with standard regimen with appropriate modifications accordingly
Non-Specific Parenchymal lesion
Antibiotics for 2 weeks if no clearance in 4 weeks
Treat with Standard regimen of ATT
Treat with standard regimen with appropriate modification (if disease is disseminated or extensive).

of 2 - 8%[36]. Since BCG cannot prevent the tubercular infection, WHO recommends BCG use to be continued as antituberculous measure[37]. However, children born to HIV positive mothers should recive BCG immunization[38], but the same should be withheld from children with clinical signs of immune deficiency[39].

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ORGANOPHOSPHATE AND CARBAMATE POISONING

J.N.Panicker M.D.;A. Chacko M.D.; S. Madhusudanan M.D.

Abstract: Organophosphate and carbamate compounds are commonly used as poisons. Clinical features of poisoning arise due to inhibition of cholinesterase and subsequent accumulation of acetylcholine in the neuromuscular junctions. Degree of poisoning can be graded based on signs and symptoms. Pseudocholinesterase assay is useful as a diagnostic tool. Antidote is atropine and its administration should be based on the degree of poisoning and dosage adjusted as per an atropinisation chart. Other measures that should be initiated include gut decontamination and use of cholinesterase reactivators. Poisoning is associated with high morbidity and mortality if not treated promptly. A review of cases and management practices enabled the compilation of a protocol for treatment.

Key words: Organophosphorus Poisoning, Carbamates, Insecticides, Organophosphate, Parasympathomimetics, Cholinesterases, Cholinesterase inhibitors, Poisoning, Atropine, Cholinesterase reactivators.

Introduction

Insecticides have been used extensively in recent agricultural practice. Because of free availability they have been misused for fulfilling homicidal and suicidal intentions. Two commonly misused insecticides are organophosphates and carbamates. Based on present management practices, a treatment protocol has been compiled.

Organophosphorus Poisoning

Organophosphorus compounds, organic esters of phosphoric acid, were first introduced by Schrader during the Second World War[1]. Though initially developed as agents for chemical warfare, today they are used mainly as insecticides[2]. India is the second largest user of pesticides in Asia[3] and amongst these pesticides, organophosphorus compounds are the most common. They are popular insecticides because of their effectiveness and rapid disintegration. Globally, they are freely available and their misuse galore; yearly, one million serious accidental poisonings and two million suicide attempts[4] result in 2,20,000 deaths[5,6].

Physiology

Acetylcholine is the neurotransmitter in the somatic nervous system and preganglionic, postganglionic parasympathetic and certain postganglionic sympathetic neurons in the autonomic nervous system. After acting at the muscarinic and nicotinic receptors, it is inactivated by cholinesterases; true cholinesterase found in neurons and erythrocytes and pseudocholinesterase in non-neural tissue and plasma. Organophosphates bind to the esteratic site of choinesterase resulting in its phosphorylation. The complex thus formed is hydrolysed slowly and the enzyme is inhibited irreversibly, thus preventing acetylcholine catabolism. Ageing, removal of the alkyl group leading to a more stable phosphorylated cholinesterase, contribtes to greater toxicity by preventing reactivation of the enzyme[1].

Atropine is a competitive inhibitor of acetylcholine at the muscarinic receptors. Oximes, cholinesterase reactivators, are quarternary ammonium compounds which combine with the phosphoryl group bound at the esteratic site of cholinesterase by a nucleophilic attack to form a soluble complex and thus setting the esteratic site free and reactivating the enzyme[2].

Organophosphorus compounds[7,8]

Highly toxic agents include parathion (Paramer), methyl parathion (Metacid), dimethoate (Rogor), monocrotophos (Nuvacron), DDVP (Vapona), Phosamidan (Dimecron), Phorate (Thimet), tetra ethyl pyrophosphate (TEPP), fensulfothion, azinphos, schraden, mevinphos, dicrotophos; moderately toxic agents include quinalphos (Ekalux), diazinon (Tik 20), dichlorovos, leptophos, thiometon, cythioate, phosmet, fenitrothion; least toxic agents for home use include mercaptothion (Malathion), temephos (Abate), phoxim (Baythion), acephate, and merphos.

Parathion acts after being converted to paraoxon and hence actions may be delayed. It is the commonest of the agents used for poisoning. Malathion has low toxicity

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and rapid detoxification. Kerosene like smell of some of the compounds is due to the solvent aromax[8].

Certain organophosphorus compounds have a therapeutic role: 0.025% diisopropyl fluorophosphate solution in peanut oil and 0.06% echothiophate have been used in managing glaucoma while dichlorovas and trichlorophone have a place as antihelminthics[5].

Symptomatology

Symptoms and signs are due to accumulation of acetylcholine and subsequent hyperstimulation of receptors:

1. **Muscarinic receptors:**manifests as increased respiratory and oral secretions, bronchorrhoea, pulmonary oedema, bronchospasm, bradycardia, miosis, spasm of accommodation, nausea and vomiting, abdominal camps and urofecal incontinence. Miosis may not be seen if reflex sympathetic overactivity secondary to hypotension predominates.
2. **Nicotinic receptors:** stimulaltion of the nicotinic receptors of the autonomic ganglia and neuromuscular junctions manifests as fasciculations, twitchings and variations in heart rate, followed by depolarising type of paralysis.
3. **Central effects:** stimulation with occasional subsequent depression of cholinergic receptors in the central nervous system (CNS) leads to giddines, anxiety, confusion, hypotension, ataxia, Cheyne-Stokes breathing, respiratory depression, convulsions and coma.

   Eye findings in organophosphorus poisoning include[1] pupillary constriction due to sphincter pupillae contraction, pupillary dilatation, spasm of accommodtion due to cillaris muscle contraction, conjuctival hyperemia, reduced intraocular tension, dimness of vision and chromolacryorrhoea, manifesting as shedding of red tears, due to accumulation of porphyrins in the lacrimal glands[8]. Pancreatitis can result from cholinergic hyperstimulation[1,11,12].

Cardiovascular system findings in organophosphorus poisoning[13,14]

1. Bradycardia: due to the action of acetylcholine on the SA node.
2. Tachycardia: nicotinic receptors in the autonomic ganglia may be stimulated due to excess acetylcholine, leading to intense sympathetic activity and tachycardia.
3. Hypotension: as a result of muscarinic receptor stimulation which results in vasodilatation, bradycardia and negative inotropicity.
4. Hypertension: as a result of increased sympathetic tone from nicotinic receptor stimulation in the autonomic ganglia.
5. Atrial fibrillation: due to severe hypoxia.
6. Atrioventricular blocks: as a result of action of acetylcholine on the AV node.
7. Ventricular Premature Contractions: due to myocardial injury or electrolyte imbalance.
8. QT prolongation and torsades de points.
9. Ventricular tachycardia.
10. Ventricular fibrillation.
11. ST and T changes in the ECG: as a result of myocardial ischemia, injury or electrolyte imbalance
12. Toxic myocarditis.
13. Myocardial necrosis due to hypoxia and coronary artery spasm induced by excess acetylcholine. Defects in myocardial perfusion have been documented using myocardial SPECT imaging[15].

Without a clue of poisoning, the presence of miosis and fasciculations in a patient points to the possibility of organophosphorus poisoning. The other possibilities are hypoglycemia especially when precipitated by alcohol ingestion and encephalitis. Constricted pupils are seen following use of opioids, brain stem lesions, during post-ictal state and as senile miosis. Fasciculations may be seen in motor neuron disease, cervical spondylosis, syringomyelia, thyrotoxic myopathy and as benign fasciclations. The patient brought with excessive oropharyngeal secretions and frothing may be mismanaged as a case of acute pulmonary oedema. Based on the symptomatology, the condition of the patient can be grouped into three-modified version of Dreisbach's classification[16]:

MILD: Nasea, Vomiting, Sweating.
MODERATE: Lacrimation, excessive salivation, miosis, fasciculaltions
SEVERE: Coma, seizures, incontinence, areflexia, apnoeic spells, ARDS.

Investigations:

1. Gastric aspirate, urine and blood samples are sent for toxicological analysis for confirmation.
2. Measurement of RBC cholinesterase is an accurate index of the degree of poisoning but facilities for assay are usually not readily available[9]. Pseudocholinesterase assay is used as an important indicator of organophosphorus poisoning but severity of symptoms does not correlate with the extent of depletion. It is more sensitive to inhibition than true cholinesterase and falls to less than 50% of normal

before symptoms and signs of toxicity appear. However severity of poisoning has been graded according to pseudocholinesterase depletion by Proudfoot[17]:

Normal Range: 5400-13200 IU
Mild Poisoning: 20-50% of normal (2160-5280 IU)
Moderate poisoning: 10-20% of normal (1080-2160 IU)
Severe poisoning: Less than 10% of normal (540-1080 IU)

Reduced levels may also be seen in parenchymal liver disease, myocardial infarction and in malnutrition. Levels return to normal within a few days to weeks while true cholinesterase levels return back to normal only after 90-120 days[1].

3. ECG: sinus bradycardia is the usual finding, but other changes can occur (vide supra).
4. Other findings: neutrophilic lecocytosis, glycosuria and proteinuria[18].

Treatment

Time means enzyme and one must act fast to save the life of the patient. The below mentioned ten step protocol is presented as a most efficient in minimising morbidity and mortality associated with organophosphorus poisoning:-

1. Ensure Airway, Breathing and Circulation
2. Decontaminate the exteriors: In view of high lipid solubility, organophosphorus compounds are easily absorbed from the skin and mucus membranes and hence all contaminated clothing should be removed and the body washed with soap and water[9].
3. Decontaminate the interiors:
   Gastric lavage: It is the most important step in management and is performed using no. 28 French orogastric tube in children or no. 40 French orogastric tube in adults using volumes of 5 mL per kilogram body weight tap water with 1:5000 potassium permanganate. It is continued till the solution coming out has the same pink colour as that going in[8,9]. Patient is kept in the Trendelenburg and left lateral decubitus to prevent aspiration. It is performed after endotracheal intubation in unconscious patients. The lavage tube should be introduced by the physician[9].
   Gastric aspiration: Nasogastric tube aspiration is initiated to remove residual poison from the stomach.
   Activated charcoal: It consists of fine black powder obtained from vegetable sources such as wood pulp and coconut shell which is 'activated' by an oxidising gas flow at high temperatures. This flow creates a network of 10-20 mm diameter pores which enhance the surface area to as much as 1000 m^2 / gram[19]. It adsorbs and hence inactivates the poison. In adults, 50-100 grams is given in 8 mL of diluent per gram of charcoal[9] with a cathartic, preferably within the first hour through the nasogastric tube, while in children one gm/kg is given. In severe poisoning, this single dose can be followed by multiple-dose activated charcoal (MDAC) whereby 20-50 grams is given every four to six hours. Advantages of MDAC include increased elimination of the poison even after systemic absorption and decreased release from the poison-charcoal complex as it passes through the gut. It is given either till recovery or fall in the plasma level of the poison to normal[20]. Adverse effects of charcoal include vomiting, aspiration and bowel obstruction. If not available, Universal Antidote, consisting of 2 parts of powdered charcoal, 1 part of tannic acid and 1 part of magnesium oxide can be used. A home substitute consists of burnt toast, strong tea and milk of magnesia in the same proportions[8].
   Cathartics: Sorbitol 1-2 gm/kg is the most effective[9]. Magnesium sulfate (30 gm in adults), magnesium citrate and magnesium hydroxide-paraffin preparations are also used. Initially 100 ml is given followed by 30 ml every 8 hours. Cathartics counter the reduction of bowel peristalsis by atropine and constipation by activated charcoal.
4. **Atropinisation:** Atropine reverses the muscarinic effects and the dose is titrated against the response of the patient. The signs of atropinisation are an inital pinpoint pupil becoming at least three-fourth dilated, and initial bradycardia becoming a rapid rate of 120 per minute, drying of the oral secretions, flushing of the face[1], psychosis induced by atropine and pyrexia. According to standard textbooks[9] 0.5 to 2 mg of atropine is given intravenously every 15 minutes till bronchial and other secretions have dried; pupil size and heart rate are not to be used as end points. Repeated doses of atropine are often necessary. This is continued so as to maintain the condition and then withdrawn judiciously. Because of inadequacies, modifications to this schedule have been suggested. Continuous infusion regimes using high doses of atropine have been proposed which can be given irrespective of quantity of poison, time of ingestion, clinical severity and pseudocholinesterase levels[21]. The method followed at this centre is atropine bolus administration till signs of full atropinisation are maintained. Dose of atropine thus determined is given as a continuous intravenous infusion every six hours. Management on subsequent days involves weaning

the patient from atropine, depending on the condition of the patient as recorded in the atropinisation chart. It is made into intermittent intramuscular injections and finally stopped. The key to successful management in such a schedule is close monitoring of the patient using an 'Atropinisation Chart' which includes time, pulse rate and rhythm, blood pressure, size of pupils and presence of oronasopharyngeal secretions. Other information is noted according to the clinical situation: level of consciousness, body temperature, presence of atropine induced psychosis, arterial oxygen saturation, single breath count and presence of adventitious breath sounds. Till the signs of atropinisation persist, monitoring is done every 15 minutes. Thereafter the patient is monitored hourly, so as to avoid missing the rebound phenomenon or intermediate syndrome. If additional atropine is required, the dosage in the subsequent atropine infusions is increased correspondingly.

Hypoxia and cyanosis are corrected prior to treatment as atropine can induce ventricular fibrillation in the ischemic myocardium[5]. Abrupt withdrawal of atropine can lead to pulmonary oedema. In children, the dose of atropine is 0.05 mg/kg intravenously.

5. **Cholinesterase reactivators:** Oximes reverse weakness and paralysis due to the action of organophosphorus compounds at the nicotinic receptors and are useful in cases where fasciculations predominate. They also act by directly detoxifying the organophosphorus molecule and by having an atropine like effect. Oximes include the commonly used 2-Pyridine Aldoxime Methyl chloride (2-PAM, pralidoxime), the more potent Obidoxime chloride and the oxime that crosses the blood brain barrier to reactivate brain acetyl cholinesterase, Diacetyl Monoxime (DAM).

   Oximes can be given as slow intravenous infusion, intramuscularly or orallly., However oral administration is not preferred because of slowness of action and intolerance. One gram of pralidoxime is given over 5-20 minutes intravenously followed by two doses of 500 mg each separated by 8 hours. Obidoxime is given 3-6 mg/kg and DAM 1-2 gm intravenously. Dose is reduced in children. Oximes reduced the necessity and/or duration of mechanical ventilation and amount of atropine used.

   Side effects include transient neuromuscular block and respiratory arrest. Rapid infusion (500 mg/mt) can cause mild weakness, blurring of vision, diplopia, tachycardia, headache and nausea. If not given within 24-48 hours of poisoning, the phosphorylated acetyl cholinesterase undergoes ageing and becomes resistant to the action of oximes. Neither atropine nor oximes are effective at reversing the CNS effects[9].
6. **Bladder catheterisation:** Indweling catherter is introduced because of the likelihood of atropine induced urinary retention.
7. **Antibiotics**
8. **Gastric mucosa protection:** Irritation of the gastric mucosa is minimised using sucralfate.
9. **Proper nursing care**
10. **Miscellaneous:** In case of seizures, diazepam 5 to 10 mg intravenously is used. In case of atropine induced psychosis, dose is reduced and haloperidol administered.

The role of dialysis and hemoperfusion is controversial though the latter has been used successfullly in parathion poisoning. Drugs contraindicated include morphine, theophyllines, succinyl choline, reserpine and phenothiazines. Fasciculations in the tongue is the last sign to disapper.

Mortality indicators include age of the patient, delay in initiation of therapy, presence of late onset fasciculations, pulmonary oedema, need for ventilatory support, prolonged QT_q interval and pseudocholinesterase levels less than 10% of normal[21,22]

Death usually occurs within 24 hours and is due to respiratory failure of varying causes:

- **Muscarinic:** Laryngospasm, bronchoconstriction, copious salivary and tracheobroncial secretions.
- **Nicontinic:** Compromised diaphragmatic and intercostal muscle action.
- **Central:** central respiratory depression.

Complications:

1. Pulmonary oedema.
2. Aspiration pneumonia.
3. Chemical pneumonitis.
4. Adult Respiratory Distress Syndrome (ARDS).
5. Rebound phenomenon: After an intial period of recovery and apparent stabilization, replase of symptoms occurs characterised by a sudden deterioration of level of consciousness and pulmonary oedema after 2-3 days. It has been attributed to release of organophosphates from tissue lipid stores, sudden intestinal absorption and toxic myocarditis[1].
6. Neurological manifestations: There are three main manifestations of neurological dysfunction following organophosphorus compound consumption:
   - Immediate cholinergic crisis: vide supra.
   - Intermediate syndrome: It is a relatively uncommon complication[23] and is attributed to pre- and post-synaptic neuromuscular junction

dysfunction[24,25]. Down regulation of the acetylcholine receptors as a result of persistent inhibition of cholinesterase may lead to this syndrome 1-4 days after poisoning. These receptors normally have a half life of 10 days but when heavily activated they become desensitised, rendering them more readily endocytosed. Recovery occurs 5-18 days later as a result of receptor synthesis[26]. The syndrome is characterised by proximal limb, neck flexor and respiratory muscle weakness, cranial nerve palsies and areflexia without cholinergic manifestations[27]. Bilateral vocal cord paralysis has rarely been reported as a sole manifestation[28]. EMG reveals tatanic fade, absence of fade on low-frequency stimulation and absence of post-tetanic facilitation[27]. Recovery occurs after 4-18 days. It is seen more with *fenthion, methamidophos, dimethoate and monocrotophos* use and does not respond to atropine. Recovery is first in the palate followed by facial muscles, extraocular muscles, improvement in respiratory distress, recovery of strength in proximal limb muscles and finally neck flexion. Outcome is usually favourable[27]. It can be prevented by prompt use of oximes. Incidence is more amongst those who receive high dose continuous oxime infusion than those receiving a low dose bolus at the time of admission[29].

- Organophosphate induced delayed polyneuropathy (OPIDP): Sensorimotor neuropathy arises as a result of neuropathy target esterase (NTE) inhibition and occurs 2-3 weeks after consumption of large amounts of certain organophosphorus compounds such as *methamidophos, trichlorphon and leptophos*. Distal limbs are usually affected. EMG reveals a denervation pattern. Recovery occurs after 6-12 months[30].

7. Chronic organophosphate induced neuropsychiatric disorder (COPIND): It consists of chronic neurological and psychiatric manifestations occurring following poisoning. It is a new entity and clinical features ad possible markers for the condition have been described[31].
8. Extrapyramidal side effects: dystonias and tremors[32]
9. Guillain-Barre syndrome.
10. Ginger-jake paralysis : demyelination and quadriparesis following exposure to triorthocresyl phosphate.
11. Neuroleptic malignant-like syndrome[33]
12. Central Diabetes inspidius[34]
13. Arrhythmias.
14. Pancreatitis[1,11,12]
15. Haemorrhagic panoesophagitis[35].
16. Transient liver dysfunction, rarely coagulopathy.
17. Platypnoea - Orthodeoxia syndrome[36].

Recent trends in management

GK 11 (gacyclidine), an antiglutamatergic drug, has been shown to counteract the neuropathology due to organophosphorus compound exposure. It is neuroprotective and reduces the number of seizures[37]. Newer oximes and different techniques for administration[38] are being developed.

Carbamate Poisoning

Carbamates include carbofuran (furadan), carbaryl (Sevin), Aldicarb (Temik), Aprocarb (Baygon), Bendiocarb (Ficam) and Propoxur[7,8]. While carbamates are also cholinesterase inhibitors, they differ from organophosphates in the following ways[1]:

- Mechanism of action - carbamylation of cholinesterase and subsequent accumulation of acetylcholine
- Rapid dissociation and hence reversible inhibition.
- Rapid elimination by serum and liver enzymes
- Less symptomatology
- Shorter duration of symptoms
- Poor CNS penetration; convulsions uncommon
- Cholinesterase assay not important because its activity returns to normal within a few hours even when symptoms persist.

Treatment is similar to that for organophosphorus compound poisoning but use of oximes is controversial[9] as reactivation is rapid and when administered at high doses, can cause neuromuscular paralysis through a weak anti-cholinesterase activity. But they can be used if a patient presents with cholinesterase inhibition and nature of the insecticide is not known or if the individual has consumed an organophosphate along with carbamate. The role of activated charcoal is controversial[39].

Conclusion

A review of cases of organophosphate and carbamate poisoning and management as well as a literature search indicates the need for a well planned protocol for treatment. This is necessary to minimise morbidity and mortality. The proposed protocol relies primarily on clinical features. Administration of atropine is based on the degree of poisoning and dosage adjusted as per an atropinisation chart. Gut decontamination, use of oximes and other appropriate measures are to be taken along with this. Complications such as rebound phemonenon and intermediate syndrome should be anticipated and treated accordingly.

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RUMINATION

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Rumination (cud chewing) is an effortless repetitive gagging, regurgitation, mouthing, reswallowing of undigested food within minutes of a meal, often with repetitive head movement. The food regurgitated into the mouth is again masticated and then either reswallowed or spit out. This act is accompanied by a more or less pleasurable sensation and without nausea or effort and occur some times after meals. Rumination in man is comparable to the same condition in certain animals. Rumination as a disorder occurs both in infants as well as in adults although in the latter it is highly under reported possibly because of the embarassment of accepting it. Clincially significant rumination is rare, making up 1% of admissions to childrens hospitals and still less for adults. But complications of electrolyte imbalance and/or malnutrition and aspiration account for 15% mortality rate.

Rumination is usually said to be of two types (a) Psychogenic (b) Self stimulated.

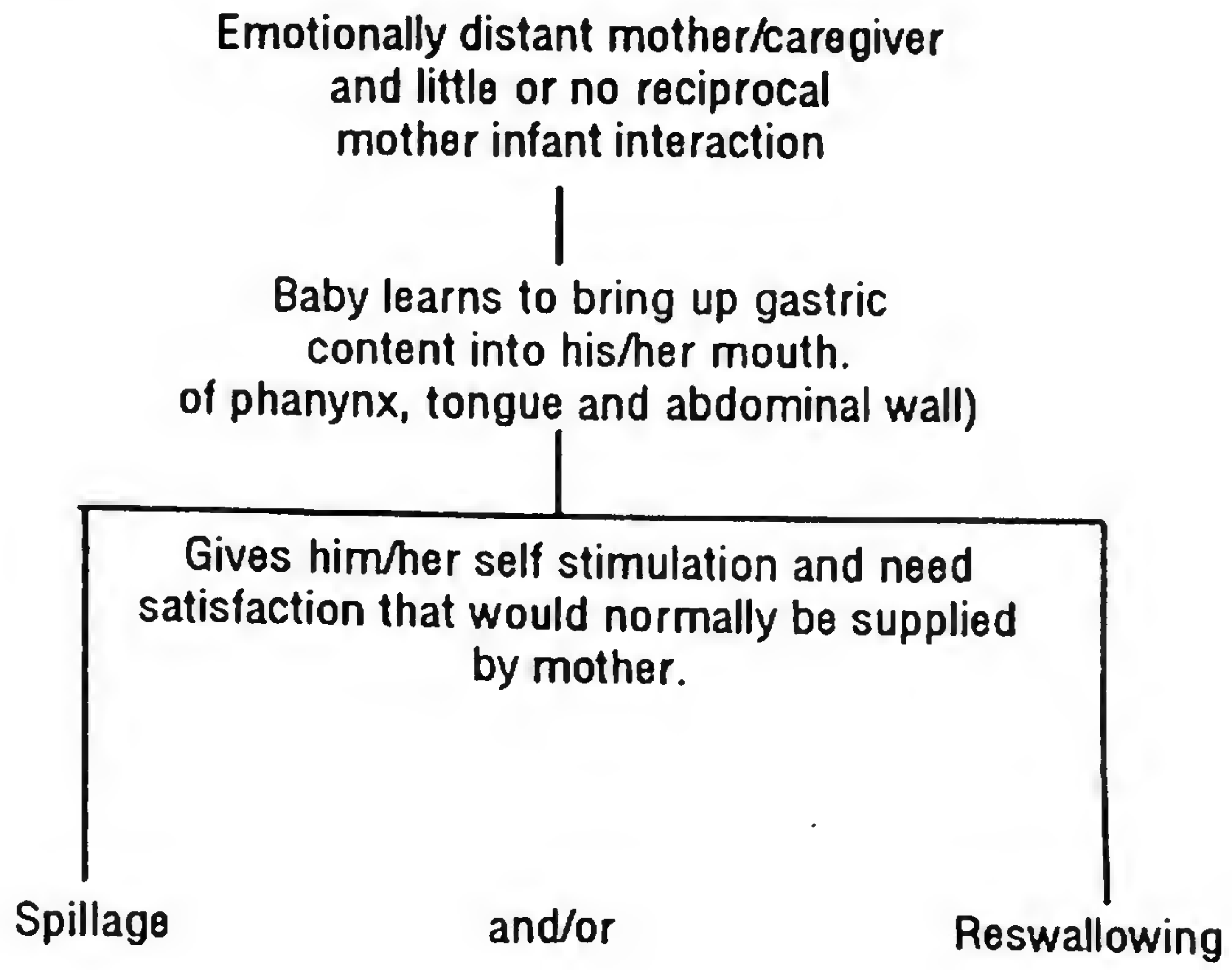
(a) **Psychogenic:** Infants with otherwise normal development but disturbed parent child relationship.
(b) **Self Stimulated:-** Mentally retarded individuals at any age and also occurs in children in the presence of nurturing parents though less commonly.

Infant Rumination

Features

- Onset between 3-8 months.
  below 3 months?
- Inanition & possible death (1/4 affected die)
- *Failure to Thrive* (FTT) which does not improve with;
  - Antireflux management
  - Formula changes.
  - Arm restraints
  - Gastrostomy feedings.
- No distress; an acquired skill
- Typically occurs when baby is awake quiet or self absorbed and in the absence of environmental stimuli.
- Often fingers or fist are inserted into mouth to initiate a gag.
  This behaviour may be a symptom of esophagitis and occur with or without GER.
- Rumination has been noted in association with *Sandifer syndrome*.

Events:


Emotionally distant mother/caregiver and little or no reciprocal mother infant interaction
Baby learns to bring up gastric content into his/her mouth. of phanynx, tongue and abdominal wall)
Gives him/her self stimulation and need satisfaction that would normally be supplied by mother.
Spillage
and/or
Reswallowing

Diagnosis

History

Mother:- H/O childhood emotional trauma. Difficult adult reationships. Family dysfunction.

Observation:

Careful observation to distinguish it from Innocent and/or nervous vomiting which are involuntary and occur as early as newborn period and mother infant relationship is normal. These occur during wakeful state or in response to environmental stimuli. *"Rumination can be observed by stealth, by peering through peepholes, between screens and so forth"*.

Barium Swallow roentgenogram:

Often reveals early reflux or a hiatal hernia.

Therapy

Temporary mother substitute or a mother like nurse to hold; socially interact and feed the infant during hours he/she is awake. Psychotherapeutic help to mother or parent.

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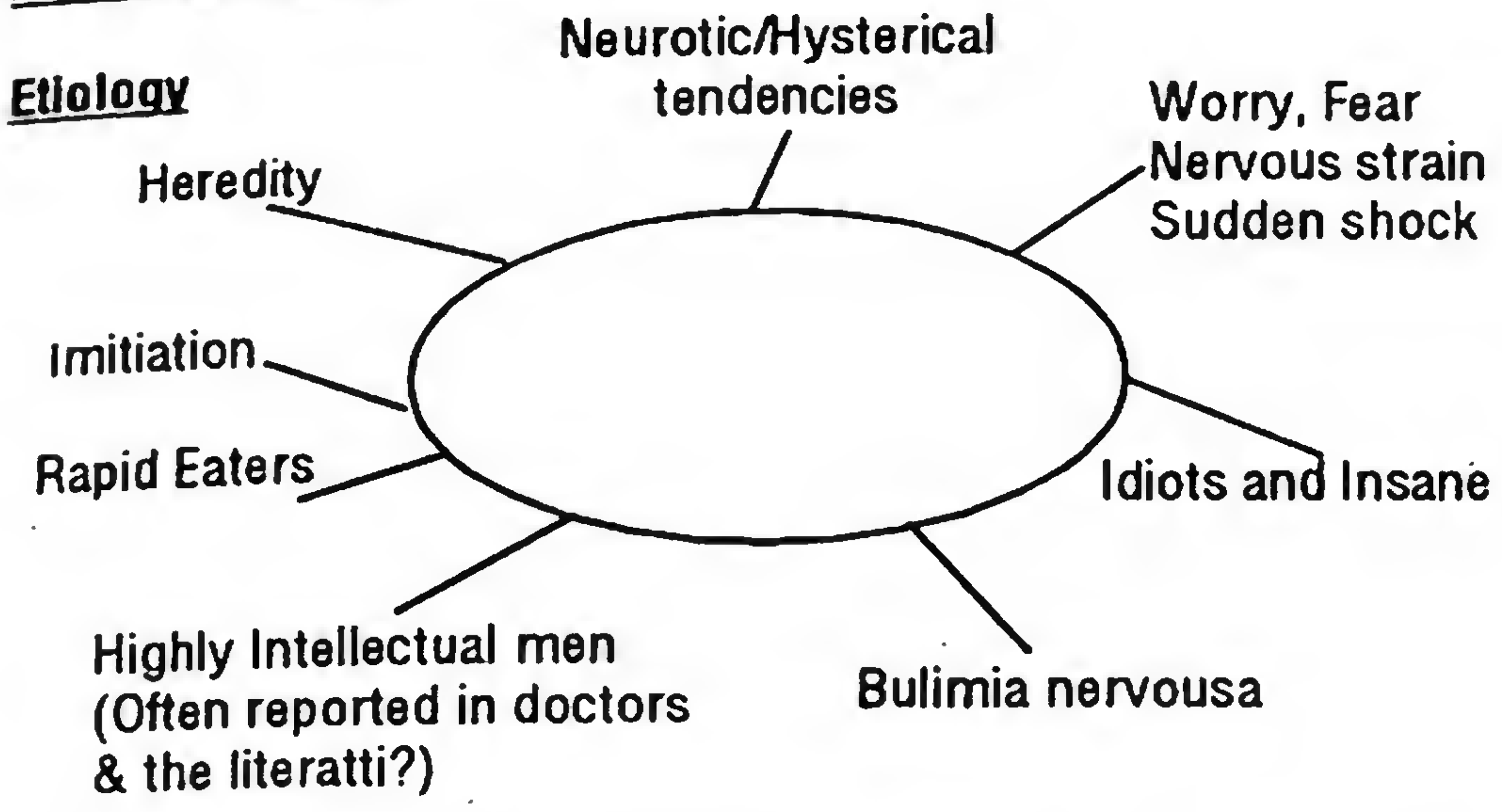
Not Primary therapies	Fundoplication.	
	Behavioural therapy e.g.	electric shock. aversive taste stimuli punishment.

Adult Rumination

Etiology


Neurotic/Hysterical tendencies
Heredity
Worry, Fear
Nervous strain
Sudden shock
Imitation
Rapid Eaters
Idiots and Insane
Highly Intellectual men (Often reported in doctors & the literatti?)
Bulimia nervousa

Roossier has reported this condition in a father and two sons and Loewe cites a family in which four members were ruminants. It has also been observed in a father of 51 and a daughter aged 14 years.

- In many cases neurotic and hysterical tendencies have been observed.
- Koerner reports a case in which a governess addicted to this habit imparted the condition to her two pupils.

Source: A System of Medicine — Sir William Osler.

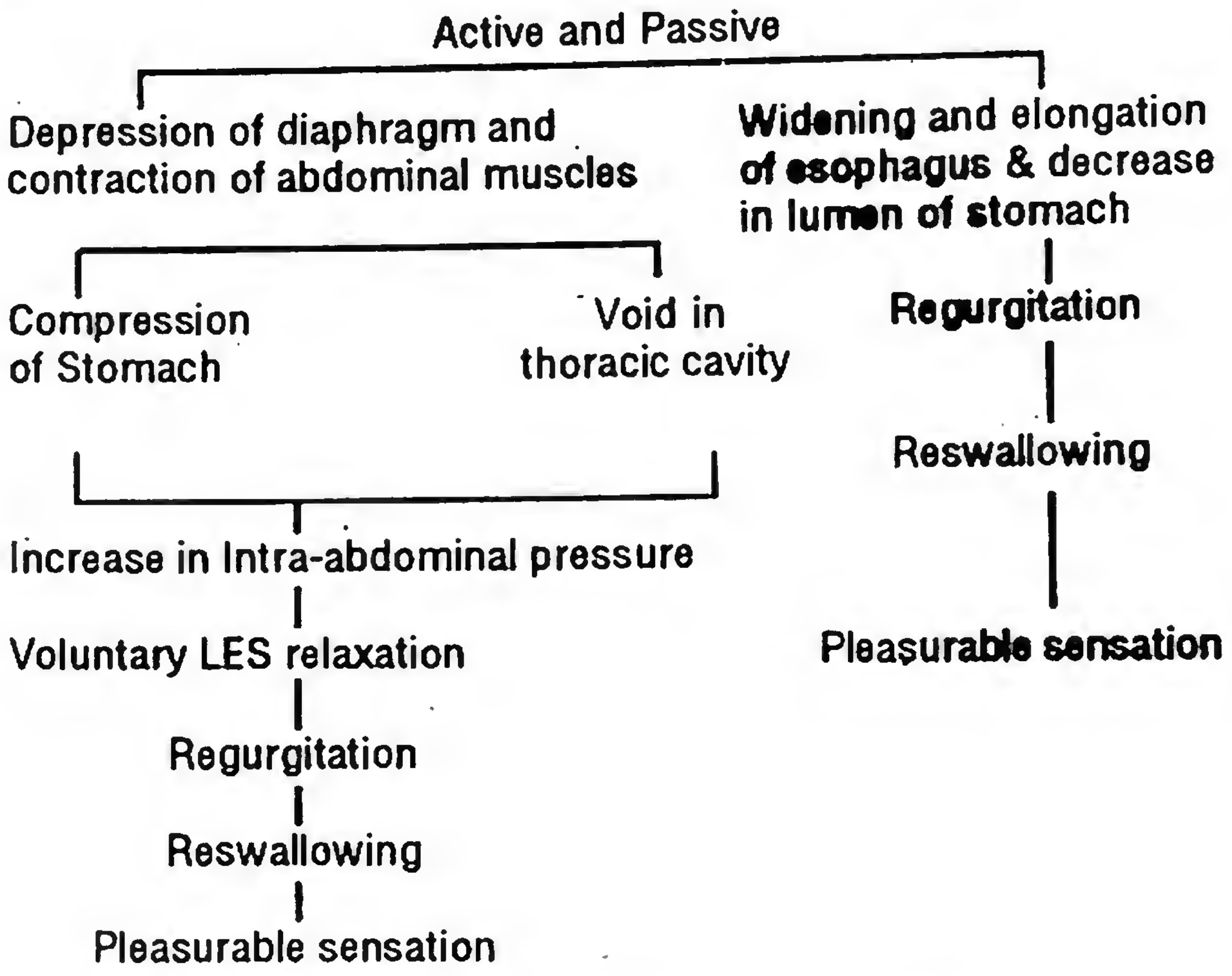
Features:

- At all ages.
- More common in males than females.
- Usually takes place during early period of gastric distension.
- Rarely occurs on a fasting stomach.
- The remastication continues as long as the regurgitant food has a pleasant taste, however, as soon as it becomes acidic (during late period of digestion) it is either reswallowed at once or ejected. Rumination may take place after every meal and last for a short period of time or extend over hours.
- Deglutition sounds remains perfectly normal.
- As a rule the general nutrition of patients suffering from this disorder is good although when large portions of all meals are not reswallowed, emaciation is produced and the general nutrition becomes markly affected.

Diagnosis:

This is made as a rule without difficulty. It differs from regurgitation in that, in the former condition, the food is again masticated while in the later this process does not take place. In vomiting, nausea and retching are present while merycism is accompanied by pleasurable sensation. This phenomenon can be clearly differentiated from a true vomiting sequence on a manometric study. One study suggests that the diagnosis can be established on clinical grounds alone in most patients and that manometry should be reserved for those situations in which the history is not typical. This disorder usually reflects a primary psychological disturbance.

Events:


Active and Passive
Depression of diaphragm and contraction of abdominal muscles
Widening and elongation of esophagus & decrease in lumen of stomach
Compression of Stomach
Void in thoracic cavity
Regurgitation
Reswallowing
Pleasurable sensation
Increase in Intra-abdominal pressure
Voluntary LES relaxation
Regurgitation
Reswallowing
Pleasurable sensation

Differential Diagnosis:

- Esophageal stricture
- Achalasia
- Duodenal Ulcer
- Congenital anomalies that affect development of GIT and pyloric valve.

Prognosis:-

This is often good especially if the patient makes the effort to overcome this habit. This condition may extend during a long priod of time, being present occasionally during the entire life or frequently disappears for a longer or shorter period to recur again following some mental strain or shock.

Treatments:-

- This consists essentially in an auto supression. In a certain number of cases the patient can be taught to overcome this disease. He should be required to eat slowly and masticate thoroughly. Three patients of a series of 24 cases of merycism studied by Sir William

Osler were cured in this way.

- The state of the gastic secretion occassionally gives a clue to treatment. HCl, is useful in cases of subacidity while alkalies are a benefit in superacidity.
- Intragastric electricity has been recommended and was of great benefit in two patients.
- In those who are much run down and weakened by disease a thoroughly regulated rest cure with psychotheraphy is most effective, three patients were cured in this way.
- Strychinine and Quinine have been recommended in as much as their taste destroys the desire to remasticate.
- Lavage has been used by Johannessen. and
- Gavage by Jurgensert.

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EXTERNAL SKELETAL FIXATION BASIC CONCEPTS, GENERAL PRINCIPLES AND TECHNIQUE

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Introduction

External fixation is a method of immobilizing fractures by means of pins passed through the skin away from the fracture site. The pins are joined outside the limb by a rigid scaffolding.

The first recorded external fixation device was described by Malgaigne in 1853, but the essential principle was recognised by Hippocrates who used leather cuffs at the knee and ankle containing sockets. Springy wooden rods were inserted into sockets to maintain the stability of the fracture. Rapid developments in the design of external fixation devices have taken place and have been extensively studied both clinically and biomechanically (Hoffmann 1938, Vidal and Merchard 1966, Audrey 1970 and Rezaian 1977). The 1970's were dominated by bilateral configurations of the external frames but clinical experience showed that they were unsafe and unsatisfactory. In 1980's unilateral configurations were evolved which showed better biomechanical properties.

The aim of this paper is to highlight the basic biomechanical principles and general surgical technique of application of the external fixator and experience of 100 patients treated by external fixator.

Classification:

External fixators could be grouped as:

1. Ring Fixators
2. Rod or Tubular fixators.

Ring Fixators: Popularized by Illizarov of the erstwhile U.S.S.R. comprises of a modular frame that can be assembled in various configurations for specific clinical situations. This fixator employs 1.5 to 1.8mm wires which are tensioned and fixed to the external rings. The details of this fixator are outside the scope of this paper.

Rod or Tubular fixators: The basic components of a conventional tubular fixator are the rods, the clamps and the pins (fig.1) assembled in either unilateral or bilateral configuration.

The rod is available in various lengths and is mostly hollow which imparts strength to it as compared to a solid bar.

The clamp fixes the external fixation pin to the rod thereby transferring the stresses from bone to the rods via pins and vice versa. Different types of clamps are available for use in various clinical situations.

a) Swivel clamp (Fig. II) This clamp alllows the pin to be placed in many directions, thus making the system versatile.
b) Rod to Rod Clamp (Fig. III) It consists of two rod holding components which can rotate and can be clamped at any angle. These clamps are used to connect a shorter rod in each main fragment with a third connecting rod, making the system modular.
c) Transverse Clamp (Fig. IV). This clamp is used in the presence of short proximal or distal bone fragment allowing pin placement in horizontal plane.
d) Add-on clamp (Fig. V). This is used as an additional support any time after frame construction.

External fixation pin (Schanz Screw) is a modified cortical screw. It is devoid of head which is replaced by a very long shaft (dia 4.5 mm). The core diameter of the Schanz screw is slightly larger than that of a corresponding cortical screw (viz. 3.4 mm instead of 3mm for a 4.5mm screw). This increases the bending stiffness of the pin approximately 1/3rd. The tip is triangular, rounded at the front the sharp at the side. The pin is designed in such a way that the threaded portion takes purchase only in the far cortex and the shaft of the pin gets engaged in the near cortex. This imparts greater stiffness to the pin because stiffness of the pin in directly related to the diameter of the shaft and not to the core of the thread.

Technique:

Before embarking on the method of external fixation the surgeon must be familiar with the various limb segments of the body. The limb segments are classified in two groups:

a) Concentric limb segments are those where bone is

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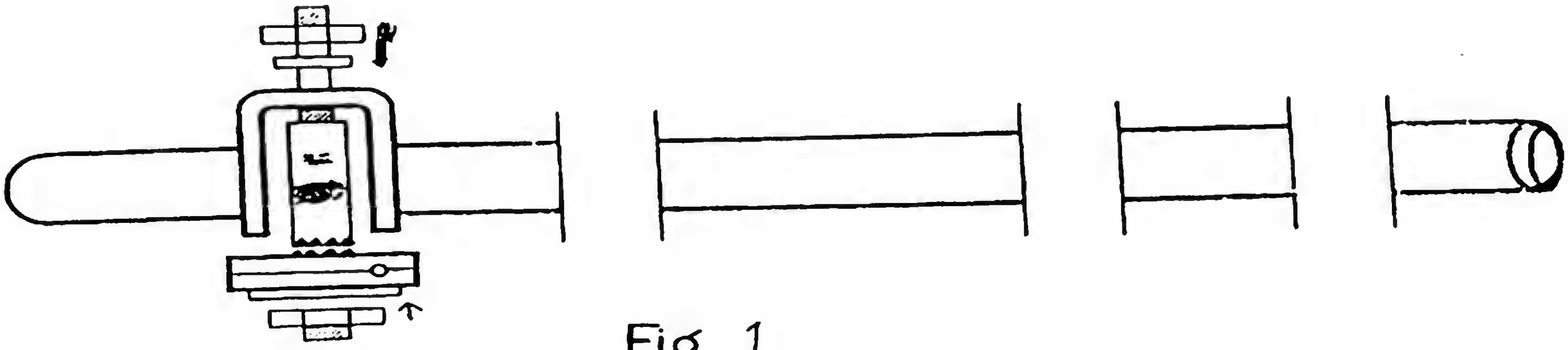

Fig 1

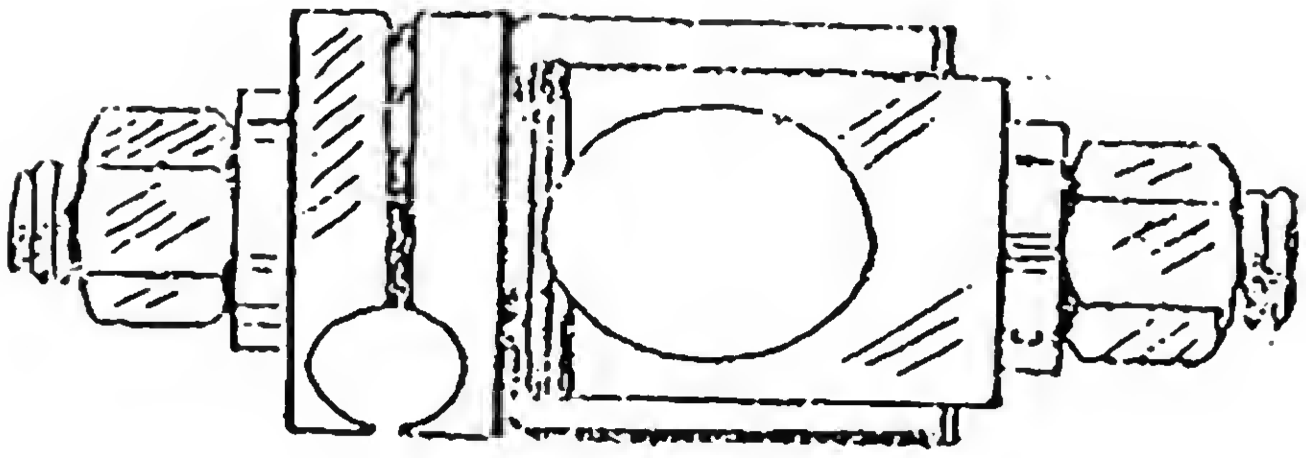

Fig II

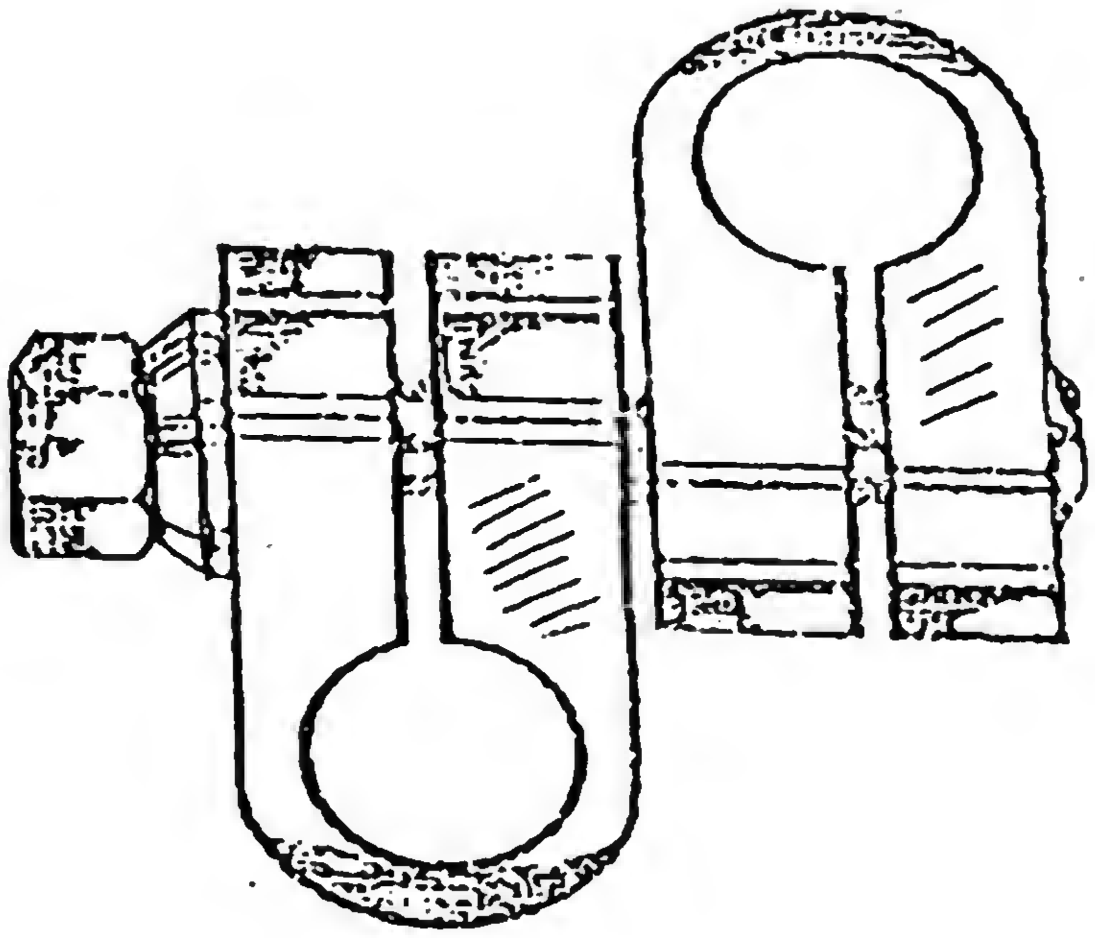

Fig III

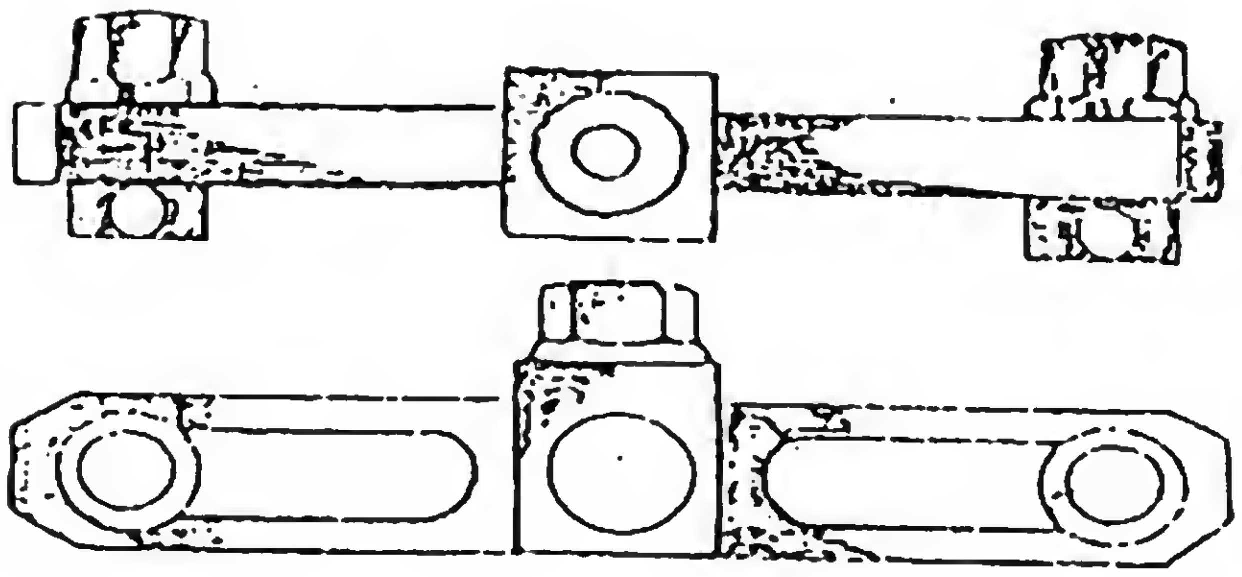

Fig IV

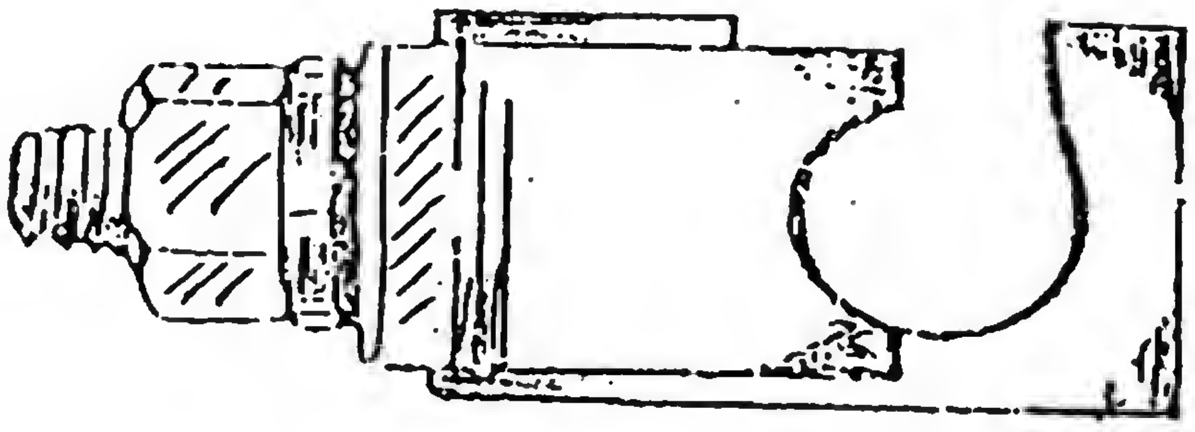

Fig V

surrounded by soft tissues on all sides. Femur, humerus, radius are the examples of this group. The Schanz Screw always passes through the muscles and the soft tissues, predisposing to high incidence of pin tract infection, muscle fibrosis and joint stiffness. Hence the fixator must be employed as a temporary stabilizer in such situations.

b) Eccentric limb segments are those where at least one surface of the bone is subcutaneous e.g. Tibia, Ulna, Metacarpal Matarsal and Pelvis. The external fixator is best suited for such situations and can be used as a definitive method of management.

Safe corridors, which have been worked out, should be followed while passing the Schanz pins. The following technique should be strictly adhered to ensure a successful outcome;

- One cm. skin incision is given at the proposed site of pin insertion and the tract of the pin is dilated with a straight haemostat.
- A trocar and double drill sleeve is passed through the tract and fixed to the bone to be drilled.
- The trocar is removed and the bone is drilled with a 3.5mm drill but preferably with a power drill, to avoid wobbling of the drill and hence an oval hole formation.
- The drilling is done in a stop and start action to avoid heat generation and thermal bone necrosis (which can predispose to PTI). The drill bit is continuously irrigated with normal saline for the same purpose.
- The inner sleeve is removed and the near cortex is overdrilled with a 4.5mm drill bit.
- The external fixator pin is inserted with a special T-handle till the tip of the pin abuts (but does not cross) the far cortex.
- The pins are first inserted as close to fracture site on either side of the fracture, as possible.
- Clamps are mounted on the pins and the rod is fixed to the clamps. By doing this insertion of the rest of the pins becomes easier and they fall in the same line.
- After inserting all the pins the rod and the clamps are tightened and stability of the fracture is ascertained.
- An X—Ray is always taken at the completion of the procedure. If instability persists, following options are available to the surgeon.
  a) Increasing the number of pins in each bone fragment.
  b) Delta frame construction.
  c) Telescopic fracture reduction.

Modular frame construction:

Modular frame is a modification of unilateral uniplanar frame. If local anatomy and soft-tissue conditions do not permit placement of the pins in one line, the modular frame constructions can safely and quickly be applied, without compromising the stiffness of the External Fixator.

Using two Rod to Rod clamps the pins can be inserted in different planes and then connected by a short 3rd connecting rod. The rods can be rotated in relation to each other and fixed in a convenient position. Thus radial nerve can be taken care of in external fixation of humerus and pin can also be placed such as to avoid areas of soft-tissue and skin loss. This also makes it possible to perform secondary soft-tissue procedures like skin grafting, especially application of cross leg flap in leg wounds. Modular frame also allows secondary adjustments simply by loosening the R-R clamps and manipulating the fracture while the assistant tightens the clamps at the opportune moment.

When planning external fixation for an individual clinical problem certain important factors influencing the rigidity of the frame should be considered. They are:

- Number of pins: More the number of pins better the stability. Minimum of two pins in each bone segment in tibia and three in femur is essential.
- Pin spread: By increasing the distance between the pins in each bone fragment, there is an increase in the bending stiffness of the fixator.
- Pin angle: Increasig the angle between the pins when viewed along the bone axis increases the bending stiffness under moments applied at 0 to 90 degrees.
- Bone rod distance (i.e. effective pin length): Decreasing the effective pin length increases the fixator stiffness as regards bending, torsion and compression. In general Bone rod distance should not be more than 4 cms.

Pin Bone Interface - a concept:

Under various loading conditions, the pins are subjected to bending. If the fracture is unstable the stresses at the pin bone interface can reach very high levels producing an yielding failure. Such stresses at the PBI can be reduced by increasing the bending rigidity of the pin, by using a pin with larger diameter and a high elasticity modulus; reducing the effective pin length or by using a bilateral frame. Weight bearing should be avoided in fractures without bone to bone contact. Surgical pin insertion technique is also very important in this respect. The pins should be inserted with a power drill. Hand drill produces wobbling leading to the formation of an oval hole and consequent poor pin purchase. Eccentric pin insertion and thermal bone necrosis due to blunt drill bit should also be avoided. In fractures which have cortical contact axial dynamization restores the cotical contact in stable fractures leading to a decrease in pin bone stress.

Dynamization of External Fixator:

It has been proved beyond doubt that some degree of micromotion at the fracture site is essential for effective healing of the fracture. The fracture can be dynamized in the following ways:

- Encouraging patient activity.
- Progressive frame dismantling.
- Progressive and controlled weight bearing.
- Loosening the clamps sliding them away from the skin, hence increasing the pin span.

Care of Extremity after External Skeletal Fixation:

1. Limb elevation on Bohler Braun frame or suspension cords tied to external fixator.
2. Splintingthe adjacent joints to avoid contracture. This can be easily done by supporting the foot in a surgical face mask made of cloth.
3. Active and passive joint mobilization after the reaction of injury is lessened.
4. Pin site care by regular removal of crusts and cleaning the sites with dilute hydrogen peroxide or spirit.
5. If the pin becomes infected or loose, remove it and insert a new pin, at a different site.
6. Regular tightening of nuts and bolts.

Present study consisted of 100 cases of open tibial fractures treated by External fixation.

44% of cases had sustained firearm and bomb blast injuries, 30% vehicular trauma and the rest were due to trauma like stone-hit and fall from height. 77% of patients had Gustilo's Type III and 23% had type II fractures. All fractures were thoroughly debrided and fixed rigidly with unilateral or bilateral external fixators. Mobilization of the adjacent joints was started within first two weeks and patients were allowed to do non-weight bearing crutch walking subsequently Primary wound closure was done in two cases and the rest required secondary soft tissue procedures like delayed primary closure, split skin grafting and cross leg flap. Bone grafting was done in 40% cases. Patients were given PTB cast after removal of the external fixator and were followed for a period of one year. Clinico-radiological evaluation was done with respect to wound healing, bone healing and functional recovery. Good results were obtained in 57% and poor and fair in 38% and 5% respectively. Osteomyelitis at the fracture site and pin tract infection were observed in 28% and 21% cases respectively. Unilateral half-pin fixator was found better as regards Range of Motion at ankle, pin tract infection, fracture stability and patient acceptability,

Conclusions:

1. The external fixator can be installed quickly especially in polytraumatized patients, without much physiological insult to the limb and without disturbing the soft tissue environment at the fracture site.
2. Soft tissue and bony procedures can be undertaken with ease while the limb isin external fixator.
3. Hybrid constructs offer greater versatility of application.
4. External fixator is of special use in the management of mass casualities.
5. Early post-operative mobilization of the adjacent joints can be started without jeopardizing the fracture stability.
6. Hospital stay is significantly minimized and patient can be intermittently sent home helping them in reducing the psychological trauma due to the injury.

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PAEDIATRIC AIRWAY ENDOSCOPY

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Abstract: A review of all paediatric endoscopies performed in a tertiary referral unit over a three-year period was carried out. Retrospective analysis of case-notes of all paediatric endoscopies performed between May 1993 and June 1996 was taken up for the study.

333 paediatric airway endoscopies were performed on 146 children, of which 52% were GP referrals and the remainder secondary referrals. 70% were diagnostic endoscopies, 30% therapeutic procedures, with the commonest indication being stridor and respiratory distres (82%). Routine chest radiographs, lateral neck X-rays, and barium swallows were unhelpful in the management of the commoner upper-airway conditions. The commonest findings were laryngomalacia (44%) and subglottic stenosis (22%) and 17% of all cases had multiple airway abnormalities. Trachesotomy was performed on 18.4%, laryngotracheoplasty on 7.5% and laryngotracheal reconstruction on 2.5%. There were no major complications in this series.

All children with airway symptoms should have a thorough rigid-endoscopic evaluation of their upper and lower airways. Radiology has a limited role in the diagnosis of the more common airway pathologies. These need to be assessed and managed in regional centres.

Key words: *Paediatric Endoscopy; Airway Obstruction; Bronchoscopy; Laryngoscopy.*

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Introduction:

Paediatric endoscopy is a complicated, often difficult group of procedures that require the involvement of both an experienced otolaryngologist and an experienced anaesthetist.

We report the results of the department of Otolaryngology, Birmingham Children's Hospital UK, in paediatric endoscopy (both for diagnosis and therapeutic), and look at the indications, findings, procedures and the overall complications. Because of its specialist interest, the Birmingham Childen's Hospital has a significant number of complicated cases that reqire more than a single endoscopic procedure. This study shows the typical activity of the department over a three year period, between April 1993 and June 1996. This study highlights how the patient population in such a specialised unit can differ so greatly from that of district general units, and that managing these patients requires a multidisciplinary approach together with a high level of clinical expertise on the part of the surgeon and the anaesthetist involved.

Material and Methods

This study is a retrospective analysis of 146 patients who underwent endoscopy at the Birmingham Children's Hospital, UK, during a 3-year period, between April 1993 and June 1996. The otolaryngology department at the B'ham Children's Hospital is a highly specialised tertiary referral unit that has wide experience in the management of syndromal children with complex problems. All patients were assessed by means of full history and examination, plain chest radiographs, basic blood tests (including haemoglobin), and endoscopy under general anaesthesia. Some patients underwent further investigations prior to endoscopy- these included computerised tomography (CT), magnetic resonance imaging (MRI), barium swallow examinations, lateral soft tissue neck radiographs, bronchograms, sleep apnoea studies and respiratory function tests. Other special investigations included chromosomal studies, electrocardiograms (ECG), echocardiograms (Echo), and angiography.

The study population includes all rigid endoscopies performed under general anaesthesia for both diagnostic and therapeutic reasons. However, procedures that were carried-out at the bedside including 'awake' and fibreoptic laryngoscopies have been excluded. All techniques involved the use of the Wolf paediatric suspension laryngoscopes, the Storz ventilating bronchoscopes, and the Hopkins (0° and 30°) telescopic system. A carbon dioxide laser was used when indicated.

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mounted by an arm on a Zeiss operating microscope.

Results:

The 146 patients consisted of 79 males and 67 females. Their age ranged from 2 days to 15 years, and the age distribution is shown in Figure 1. Of these 146 cases, 75(52%) were referred from general practitioners, 25(17%) from other departments within the Birmingham Children's Hospital, mostly paediatrics, and another 45(31%) from otolaryngology departments in other hospitals.

The most common indications for endoscopic evaluation were stridor and respiratory distress, and this affected 121(82%) patients. Many of these patients with stridor also had other symptoms, including 26(17.8%) with dysphonia. Other indications for endoscopy included feeding difficulties 17(11.6%), 2 difficult intubations during routine anaesthesia, difficult decannulation after tracheotomy[1], haemoptysis[1], and 3 with obstructive sleep apnoea (OSA).

All patients had chest radiographs performed, 81 had barium swallows, 16 had lateral soft tissue neck radiographs, 3 had chest CT (computerised tomography), 6 had MRI (magnetic resonance imaging) of the head, and 1 had ultrasound of the neck. In addition, 26 required histopathology, 7 patients had cardiac investigations includig ECG, Echo, Angio, or Cardiac Catheterisation, 10 had respiratory function tests, 3 had sleep studies, 2 had bronchograms, 1 had chromosomal studies, and 1 had a metabolic profile. None of the chest radiographs and lateral necks performed were helpful in making a diagnosis.

Table-1: Tracheostomy Group

Reasons for tracheostomy	Number
Subglottic stenosis	12
Cystic Hygroma	1
Subglottic Haemangioma	2
Laryngeal Web	1
Laryngeal Web+ Congenital subglottic stenosis	1
Laryngotrachebronchial papillomas	1
OSA	1
Congenital bilateral vocal cord	2
Prologned ventilation	1
Treacher-Collins Syndrome	1
Crouzons Syndrome	2
Tracheobronchomalacia	1
Laryngomalacia	1
Pierre-Robin Syndrome	2
Marshal-Smith Syndrome	1
Dysmorphic	1
Di-George Syndrome	1

The 146 patients underwent a total of 333 endoscopic procedres. 70.5% of all procedures were diagnostic, whilst the remainder were therapeutic. Of all the procedures, 143 were direct laryngoscopies, 105 laryngotreoheoscopy, 81 laryngo-tracheo-bronchosocopy, and 4 laryngoscopy with oesophagoscopy. 126(86.3%) patients had positive findings on endoscopy, whilst the remaining 20(13.%) all had normal endoscopies. 105 patients (71.9%) only required a single procedure each; whilst the remaining 41 patients required the remaining 228 procedures between them. Of the patients that had therapeutic endoscopies 91 (39.9%) required the use of the laser to excise papillomas, haemagiomas or other lesions. Out of the 146 patients, 32(21.9%) had trachesotomies and the reasons why are shown in Table-1.

Table 2 shows the endoscopic findings grouped according to their pathology in order of incidence. (NB several patients had more than 1 pathology).

Table-2: Diagnosis with positive endoscopic findings and negative endoscopy

Positive Endoscopic Findings	n	%
Laryngomalacia	44	30
Subglottic stenosis	22	15
Respiratory papillomatosis	11	7.5
Congenital vocal cord palsy	8	5.4
Syndromal (n=8)		
Crouzons	3	2
Pierre Robin	1	
Goldenhars	1	
Marshal smith	1	
Di-George syndrome	1	
Treacher Collins	1	
Vascular rings	5	3.4
Laryngeal web/cleft	4	2.7
Vascular malformations (Haemangiomas, lymphangiomas((n=3)		
Tonge base + Floor of mouth	1	
Tongue + Supraglottis	1	
Sublottis	1	
Vocal cord nodules	3	
Iatrogenic vocal cord palsy (post-cardiac surgery)	3	
Croup	3	
Vallecular cyst	3	
Intubation granuloma	2	
Subglottic cysts	2	
Foreign bodies (Oesophagus)	2	
Cystic hygroma	2	
Bronchopulmonary dysplasia	1	
Negative Endoscopy		
Idiopathic	10	7
Chest problems - Pneumonia, asthma, nocturnal cough	5	3.4
Obstructive Sleep Apnoea (OSA)	3	2
Dysmorphic features	1	
Choanal atresia	1	

Of the 41 patients requiring multiple procedures, 22(15%) had subglottic stenosis, 11(7.5%) had respiratory papillamatosis, 4 had laryngeal webs, 2 had subglottic mucous retension cysts, and 2 had cystic hygromas of the neck that were found to be extending into the larynx. Most of these patients required 2 to 4 procedures each, but the patients with respiratory papillamatosis required many more. The mean number of therapeutic endoscopies that patients with papillomatosis required was 8, with a range of 2 to 22.

In this population there were 31(31%) patients who had disease affecting more than one anatomic site in the airway. Many patients had multi-site involvement from the same pathology,. the commonest of which was respiratory papillamatosis. However there were 20(13.6%) patients who had multiple pathologies i.e. "synchronous airway lesions" that were diagnosed of causing significant symptoms. These are shown in Table 3. (NB tracheomalacia and bronchomalaclia are considered here as the same disease process, but with 'multisite' involvement).

Table-3: Number of patients with multiple pathologies and/or multisite involvement

Lesion	Number of Patients
Respiratory papillomatosis	11
Laryngomalacia + tracheobronchomalacia	2
Laryngomalacia + cleft palate + small mandible	1
Laryngomalacia + pulmonary artery stenosis	1
Laryngomalacia + aberrant right upper lobe bronchus	1
Laryngomalacia + tracheomalacia	1
Laryngomalacia + laryngeal web	1
Laryngomalacia + left vocal cord palsy + tracheomalacia	1
Subglottic + glottic stenosis	1
Subglottic stenosis + false cord adhesions	1
Subglottic stenosis + over hanging epiglottis	1
Subglottic stenosis + Intubation granuloma	1
Subglottic stenosis + web	1
Tracheobronchomalacia + stenosis left main bronchus	1
Tracheomalacia + Crouzons syndrome	2
Tracheobronchomalacia + cleft larynx + Hypoplastic right main bronchus	1
Left vocal cord palsy + vascular ring	1
Left vocal cord palsy + tracheomalacia	1
LEft vocal cord palsy + subglottic haemangioma	1

Many of the patients required further surgery after their endoscopic procedures. These are shown in Table 4.

There were a total of 11(7.5%) complications associated with the 333-endoscopy procedures performed. They are divided into perioperative[5], early postoperative[4], and postoperative[2]. Table-5 shows the complications together with their subsequent management and outcomes.

Table-4: Further surgical procedures required

Procedure	n
Tracheotomy	27
Cricoid split	11
Laryngotracheoplasty	11
Ts/As	7
Laryngotracheal reconstruction	3
Change of Laryngeal Stent	2
Choanotomy and nasal dilatation	1

Table—5: Complication

Perioperalive	n
Minor injuries to gums/upper lip	2 (both resolved completely)
Transient cardiac arrhythmias (anaesthetic)	3 (settled prodecure and did not require intervention)
Immediate	
Stridor	4 (I had mild laryngeal oedema settled without intervention; 2 had laryngeal oedema which settled with steroids quickly; 1 patiet with pre-existing stenosis required intubation and ventilation for 24 hrs.)
Delayed	
Anterior Laryngeal Web	2(subsequently lasered)

Discussion:

Paediatric airway endoscopy is one of the most clinically challenging areas of otolaryngology that needs specialised training before it can be performed safely. This is because endoscoping children with potential airway obstruction is fraught with hazards particularly due to the associated problems of paediatric anaesthesia, the significantly smaller paediatric airway, and the reduced cardiorespiratory reserve of children. In addition, such a selective group of patients may have complicating factors such as coexisting medical conditions, the presence of anatomical variations and the added risk of multiple developmental abnormalities (e.g. small mandible or poor development of the mid-face). Because of these factors it is essential that paediatric endoscopy is undertaken in tertiary referral centres by highly trained surgeons and anesthetists[1-5]. The method of anaesthesia and endoscopy needs to be tailored to the needs of that particular patient, for the particular condition, and also whether the procedure is emergency or elective[1].

Of the 46 patients reviewed, nearly half were referred either from otolaryngology departments in other hospitals (31%), or by specialists at the B'ham Children's Hospital (17%). The remainder were referred from general practitioners. As one would expect, the commonest reasons for referring were either stridor or respiratory distress, which accounted for 82%. This compares with the results of other series[6]. Two patients were referred due to difficult intubation, of which 1 had a large valecullar cyst requiring surgery and the other was normal. The patient who was difficult to decanulate following tracheostomy had developed subglottic stenosis, and required repeated endoscopy. The 3 patients with OSA uunderwent endoscopy in order to exclude laryngomalacia prior to undergoing adenotonsillectomy, because laryngomalacia may be a cause of sleep apnoea[7]. Because the B'ham Children's Hospital is a tertiary referral centre, it is not surprising to find that 6% of patients undergoing endoscopy had well known congenital syndromes, and that a total of 13.6% had multiple pathologies.

Routine imaging studies are of little use in the diagnosis of the commoner airway problems, and this is supported by our findings[8]. In fact we recommend that all children have a routine chest X-ray which will detect a few gross abnormalities, and that further radiological investigations be performed only if particular abnormalities are found at endoscopy.

Out of all the patients, only 5 required emergency procedures. Two patients had swallowed foreign bodies, which were retrieved by oesophagoscopy, and 3 patients who had croup (viral laryngotracheobronchiolitis). These are very few emergencies in a 3-year period, particularly for foreign bodies, and this is because they are referred to predominantly to secondary referral units. Hoeve (1991)[6] in his series of 1332 endoscopic procedures, found a total of 90 foreign body bronchs over an eight year period.

It has been suggested that rigid endoscopy may not be indicated in all cases of paediatric stridor[9]. However in our series we found that 21.2% patients had multiple pathologies and/or multisite involvement, of which 11 were secondary to papillomatosis and another 20 patients (14%) who had multiple pathologies in different areas. This is despite counting tracheomalacia and bronchomalacia as a part of the same disease process. It is particularly interesting to find so many patients with laryngomalacia also affected with other pathologies (15.7%). This provides a startling insight for all surgeons who have performed laryngoscopy, diagnosed laryngomalacia, and not continued with the examination of the rest of the upper aerodigestive tract. Holinger (1980) reported that nearlly half of all children with stridor had more than one congenital malformation, whereas in our population this was found to be 21%[10]. Because of these findings, it has become routine practice in our department to perform 'panendoscopy' i.e. the routine examination of the cavity, oropharynx, hypopharynx, larynx, postnasal space, trachea and bronchi.

Majority of our patients (86%) had positive findings on endoscopy. While as the incidence of negative endoscopy in our series was 16%. This compares with the results of other series[6].

From our results it appears that childen who undergo endoscopy fall into two broad categories. The first include generally healthy children without any severe abnormalities or concurrent disease who present with specific symptoms. This group usually only require single procedure and either have no obvious abnormality discovered, or a single defect that can be treated accordingly. The other group comprise of patients that have far more complicated conditions, either developmental abnormalities or serious defects of the airway, that may be multifocal or due to multiple pathologies (i.e. "syndromal"). This group is therefore far more complicated to manage, and many of them require multiple endoscopies.

Considering the significant number of procedures performed, the complication rate of 3% in this series is comparablle to that of other workers. Hoeve reported 1.9% in a series of 1332 laryngobronchoscopies[6], Friedman 1.6% in 616[11] and Godfrey 2.5% in 364[12]. There were no mortalities directly related to these procedures, although six patients died more than 6 months after having endoscopy, and all these deaths were related to severe congenital cardiac defects. The 3 cases of transient cardiac arrhythmias were probably related to anaesthesia. Of the 4 cases of stridor, three were due to laryngeal oedema that settled quickly, and the fourth had a pre-existing subglottic stenosis that required overnight ventilation; and the two laryngeal webs were successfully treated with laser. In fact there were no long-term sequelae of endoscopy after any of these 333 procedures. It is therefore reasonable to say that paediatric endoscopy is a safe procedure in experienced hands.

Conclusions

We concluded the following:

1. All children with airway symptoms should undergo rigid endoscopy.
2. Routine radiology has a limited role for screening of the commoner airway abnormalities in the paediatric age group.

3. We believe these procedures should be performed in regional centres.

Acknowledgments

We would like to acknowledge the help and guidance provided by Mr. K. Pearman and Mr DW Proops (Concsultant Paediatric Otolaryngologists, B'ham Children's Hospital, Birmingham UK).

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Dr. G. M. Malik

TYPHOID HEPATITIS IN MULTIDRUG RESISTANT SALMONELLA TYPHI INFECTION

Gazanfar Ali M.D.; Samia Rashid M.D.; M.A. Kamili M.D.; Manoj Kumar M.D.; G.Q. Allaqaband M.D., FRCP

Abstract: A prospective study over a ten year period (1988-1998) was conducted to analyse the occurence of typhoid hepatitis, 993 multidrug resistant, culture positive salmonella typhi patients were seen. Liver function tests were done in all. Serology for hepatitis A,B,C & E and liver biopsy was done in patients with icteric hepatitis.

94 patients (9.3%) had evidence of hepatic dysfunction (71 patients with anicteric hepatitis and 23 with icteric hepatitis including one patient of fatal hepatic eneephalopathy). Serology for hepatitis A,B, C and E was negative in 23 patients with icteric hepatitis while liver biopsy showed patchy hepatocyte necrosis with mononuclear cell infiltration in 45 patients and classical typhoid nodules in one patient. It was normal in six paients.

Typhoid hepatitis is uncommon. The prevalence of hepatitis in MDR typhoid was 9.3%. Hepatic encephalopathy is rare in typhoid hepatitis. Liver biopsy in majority shows patchy necrosis with mononuclear cell infiltration. This study is the largest series of typhoid hepatitis in multidrug resistant typhoid fever studied over a decade.

Key words: Typhoid Hepatitis; Salmonella Typhi; Multi Drug Resistence.

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Introduction:

Typhoid is an old disease affilicting humans and is prevalent in the under developed countries of the tropics and the South-East regions[1,2]. Multidrug resistant typhoid fever has become endemic in India after the first report of its occurence from Asian Sub-continent[3]. In an analysis of 993 blood culture positive multidrug resistant Salmonella typhi patients, we observed many uncommon and rare compications[4-6]. Thereare only occasional reports of liver involvement in typhoid[7-9]. This study describes for the first time the liver involvement in adults with multidrug resistant salmonella typhi infection which has not been reported so far.

Materials and Methods:

This study was conducted over a period of ten years from August 1988 to August 1998 on MDR typhoid fever patients who developed hepatitis. A detailed history was obtained in every case. The sole inclusion criterion was positive bacterial culture for slamonella typhi. Of 1223 cases diagnosed clinically (males 788, females 435; aged 18-55 years) as typhoid fever, 993 patients who were culture positive (males 647, females346; aged 18-54 years) were included in this study. The clinical study included detailed examinations at and during hospital stay. Investigations included blood tests for haemogram, ESR, platelet count, widal test, kidney function tests and liver function tests. Other investigations were chest skiagram, urine and stool cultures. Serological tests for hepatitis A,B, C and E were done in all 23 patients who presented with icteric hepatitis but not in the 71 anicteric patients with hepatic dysfuunction because clinical suspicion of hepatitis was not entertained. Immuno—assay studies for detection of IgM anti-HAVand HBsAg were done for hepatitis A and B first generation ELISA, Anti-HCV and anti-HEV antibodies were measured using second generation ELISA kit of orthodiagnostic system (Chiron Corporation, USA) and Abbot Diagnostic System (Chicago, USA). All the 23 patients with icteric hepatitis received liver biopsy.

Specific therapy was given in accordance with the sensitivity results. Therapeutic regimen was modified in the mid-course when clinical response to the specific therapy was regarded as inadequate or when complications occured. Treatment was given for a period of two weeks.

Results:

All patients were blood culture positive for salmonella typhi. Some strains of rare phage types USV$_2$-type II and untypable were encountered. The salmonella typhi strains were found to be resitant to conventional antibiotics like chloramphenicol, aminopenicillins, co-trimoxazole, cephalexin, gentamicin and furoxone and sensitive to fluoroquinolones (Ciprofloxacin, Norfloxacin and pefloxacin). Some strains were sensitive

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to cefotaxime also. In Kashmir typhoid has been multidrug resistant since 1983. Out of 993 culture positive cases of typhoid fever, 94 patients (9.3%) had hepatic dysfunction. Among them, 71 patients (7.1%) ha anicteric hepatitis with a two to three fold rise in serum transaminases (table I) while 23 had icteric hepatitis. The 23 patients (2.2%) who aged 18-34 years (14 males, 9 females) and presented with fever, jaundice and hepatomegaly underwent liver biopsy. All these 23 patients developed high grade fever and yellowish discolouration of eyes of 3-8 days duration. There was no history of anorexia, nausea or vomiting or prodromal symptoms suggestive of viral hepatitis. There was no past history of drug intake, jaundice, transfusions or parenteral injections. On physical examination at admission, these patients were febrile and jaundiced. They had no signs of hepatic encephalopathy. The heart and lungs were normal. All patients had hepatomegaly and 10 patients also had spleenomegly. Other clinical details are given in table II. Serology for hepatitis A, B, C and E was negative in all. Of these 23 patients, liver histology was normal in six, while hepatitis characterized by patchy necrosis and mononuclear cell infiltration was seen in 16 patients. One patient had classical typhoid nodules (Fig.I).

With one exception, all these 23 patients recovered completely. An 18 years old girl (Case I, Table II) who became afebrile on 7th day of therapy, developed on the 14th day deepening jaundice and asterexis and lapsed into coma. The repeat liver function tests on 15th day revealed a serum bilirubin of 22 mg/dl, AST 600 u/L, ALP 23 KA units and prothrombin time of 18 seconds against a control of 12 seconds. She was managed as fulminant hepatic failure with grade 4 hepatic encephalopathy but died 3 days later. Her liver biopsy done on 6th day of admission showed classical typhoid nodules and patchy hepatic necrosis.

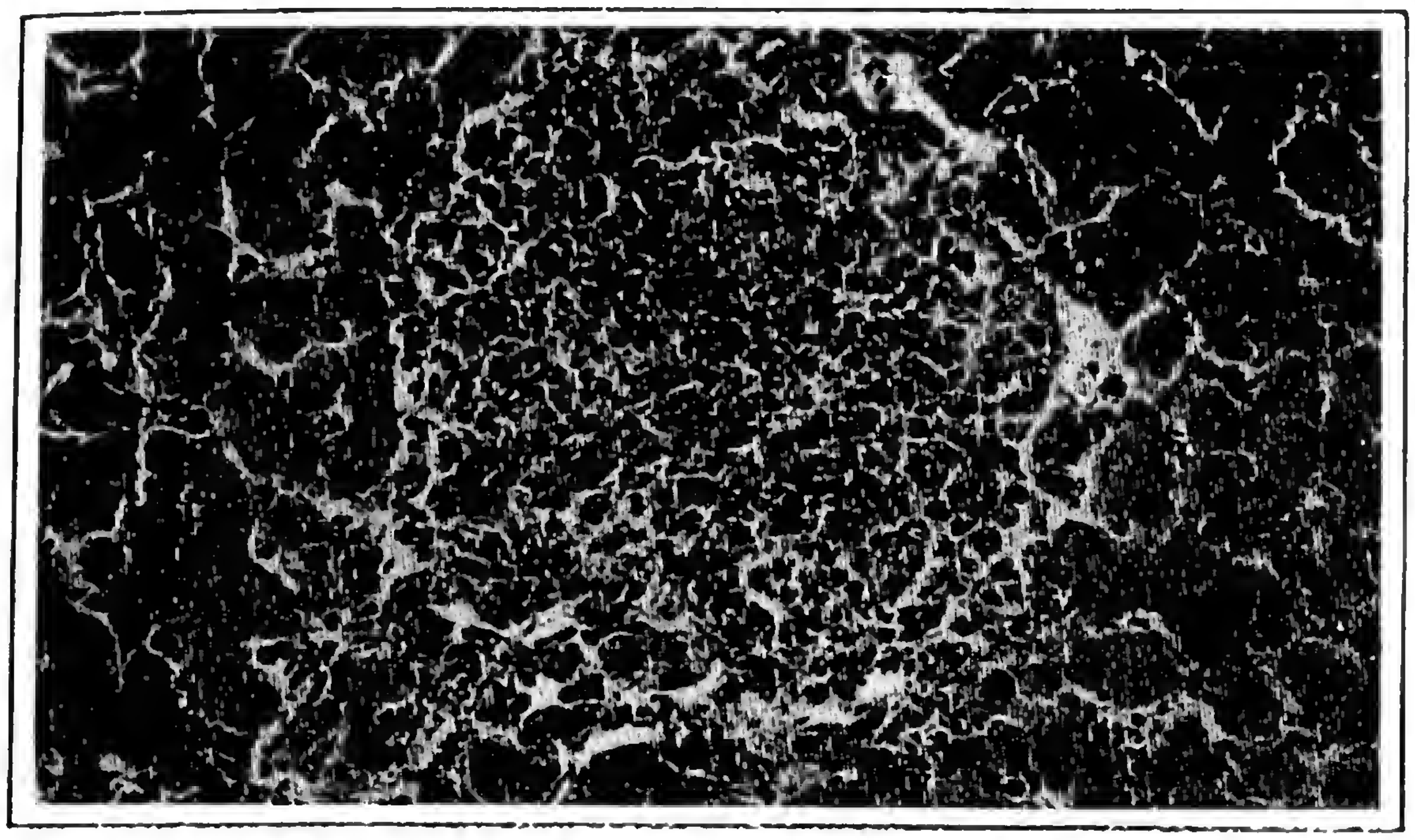

Table-I Bio-chemical alterations in 71 patients with anicteric hepatitis.

Test Value	s. Bilirubin mg/dl	% of Patients AST (Iu)	ALT (Iu)	ALP KA units)
1 N	100	0	0	47
2 N	0	39	40	20
3 N	0	28	28	3
>3 N	0	4	3	0

N: Normal (20 - 40 Iu) AST: Aspartate amino-transaminase. ALT: Alanine amino—transaminase ALP: Alkaline phosphatase.

Discussion:

Jaundice is uncommon in typhoid fever and rare[8,10] is the presenting manifestation of the disease. It has been observed in only 0.4% of cases in a series of 2476 patients,[10,11] but was found in 2.2% of patients in our series. Hepatic encephalopathy with a fatal outcome which is rare in typhoid fever[11-13] was seen in one of our patients. The possibility of drug related cholestasis was excluded by the negative drug history and normal levels of ALP in all the patients. We observed that AST and ALT levels in icteric typhoid hepatitis were relatively low as compared to those of classical acute hepatitis. The higher incidence of typhoid hepatitis in the present series could be due to higher virulence of the endemic multidrug resistant strain of salmonella typhi. It is believed that high concentrations of endotoxin is liberated at the site of multiplication of salmonella typhi in the liver and provokes granulomatous or mononuclear inflammatory response[1,14]. Tolerance to

Table-II: Age and Sexwise distribution of liver function tests of 23 patients with Jaundice.

S.No.	Sex.	Age (years)	S.Bilirubin mg/dl	Albumin (g/dl)	Globulin (g/dl)	AST u/L	ALT u/L	ALP K.A. Units.
1.	F	18	14/20	3.0	2.2.	510	460	24
2.	M	18	5.5/8	5.1	2.6	300	300	15
3.	M	20	4/6	3.8	2.0	160	160	15
4.	M	20	3.8/6	4.5	2.0	170	170	11
5.	M	21	3/5	4.8	2.3	120	100	18
6.	M	21	3/5	4.5	2.6	170	188	12
7.	F	21	3/5	4.0	2.8	190	184	13
8.	F	22	5/7	5.0	2.3	120	120	13
9.	F	22	4/7	5.0	2.7	120	100	20
10.	F	28	3.5/6.0	4.4	2.0	180	186	12
11.	M	28	4/6.5	4.2	2.2	110	100	11
12.	M	29	6.5/9.0	3.6	2.5	140	140	13
13.	F	29	6/9.0	3.4	2.3	340	315	15
14.	F	30	3/5.0	4.6	2.6	190	190	12
15.	F	30	6/9.0	4.0	2.9	140	130	22
16.	M	30	5/7.2	5.2	2.1	184	116	12
17.	M	31	8/11.0	3.8	2.3	320	300	19
18.	M	31	6/10.0	3.0	2.8	266	240	20
19.	M	32	4.5/10.0	4.6	3.2	190	100	11
20.	M	32	8.2/12.0	3.4	2.2	400	400	18
21.	F	32	7/10.5	3.6	2.5	240	240	12
22.	M	33	4.7/7.0	4.2	3.4	180	160	13
23.	M	34	8/12.0	3.9	2.4	320	320	10

this local exposure of endotoxin does not occur as it does for systemic liberation of endotoxins[1]. Liver biopsy in majority of cases shows patchy necrosis with mononuclear infiltraters. Occasionally classical 'typhoid nodules' may be seen.

In the present study, the prevalence of hepatitis in MDR typhoid was 9.3%: 2.2% developed icteric hepatitis and 7.1% had anicteric hepatitis. These results are similar to those reported in children also[15]. Asymptomatic hepatitis has been reported as a common occurence in typhoid fever with minor elevations of AST and ALT and uncommonly associated with jaundice[16,17] but in the present study only 7.1% had asymptomatic hepatitis. Many complications of typhoid fever may coexist in the same patient[6,11,13]. Since typhoid fever remains a major health problem in developing countries and with multidrug resistant strain prevalent all over India[3,6,18] and elsewhere[19] with high morbidity and mortality[5,6,18] recognition of typhoid hepatitis is important. It should be considered in the west also due to increasing inter-continental air travel[19].

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COMPOSITE GRAFT TYMPANOPLASTY

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Abstract: Out of fifty six ears with chronic suppurative otitis media fit for tympanoplasty, 23 were subjected to grafting with composite tragal perichondrium cartilage autograft and 23 to grafting with temporal fascia and rest 10 ears underwent canal wall reconstruction along with. Tympanoplasty type I using temporal fascia was successful in 17 (74%) ears while tympanoplasty using composite cartilage graft was successful in 20 (91%) ears. Composite graft procedure gave better functional improvement, helped in reconstruction of canal wall and was useful in elimination of retraction pockets. Therefore composite cartilage tympanoplasty offers possibility of a regourous tympanic membrane reconstruction.

Key words: Chronic Suppurative Otitis Media, Graft: Tympanoplasty

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Introduction:

Since Wullstein coined the term tympanoplasty in 1953, great strides have been achieved in the plastic procedure for reconstructive middle ear surgery. In 1956, Zollener, first used fascia lata to close the perforation. In 1958, Heerman was first to use temporal fascia. The advantages of connective tissue over skin as transplant soon became evident in higher percentage of successful closures.

The use of tragal cartilage in ear surgery is an important development. Tragal cartilages easily accessible, convenient to fashion, sufficiently rigid for sound conduction,and provides a viable autograft material that can survive in a relatively avascular environment. The use of this material is advantageous in centers where other modern prostheses are not available (Mundada and Jaiswal, 1989). Over the years it has become apparent that the integrity of the septum, the posterosuperior canal wall and annular rim play a vital role in the prevention of posterior tympanic membrane (TM) retraction pockets.

However, it is this rigid quality of the composition cartilage that has led many to anticipate, a significant conductive hearing loss when using it to reconstruct the T.M. Because little has been reported in the literature comparing hearing results using cartilage with results using temporalis fascia. Therefore a study was undertaken at our hospital, firstly to compare the take rate of tragal composite cartilage perichondrium autograft over temporalis fascia. Secondly, to compare hearing gain in the postoperative period between perichondrium composite autograft and temporalis fascia.

Material and Methods:

The retrieved charts of 56 patients with perforation of TM, who underwent tragal composite cartilage and temporalis fascia tympanoplasty from the mateial of study. Fifity six earswere followedupto 12 months. Out of these 10 ears had retraction pockets and associated dehiscence of scutum and posterior canal wall. The patients were selected on the following criterion.

(i) All the ears had defect involvig the tympanic membrane.

(ii) Absence of pathologies like unhealthy mucosa, granulations, polyps, cholesteatoma or sensorineural hearing loss.

(iii) Absence of of adjacent infective focus in sinuses,tonsils etc.

(iv) All the ears had been dry for a minimum period of four weeks.

All patients selected for surgery were subjected to otomicroscopic exam, pure tone audiometry (ISO standard) and assessment of eustachian tube function. There were 38 males and 18 females. The patients age ranged between 18 and 55 yeas.The patients weregrouped as follows:

a) Group I: Ears undergoing tympanoplasty typ I (Wullstein) using temporalis fascia autograft.

b) Group II: Ears undergoing tympanoplasty type I using tragal cartilage perichondrium composite autograft.

c) Group III: Ears undergoing posterior canal wall and scutum reconstruction using cartilage perichondrium composite autograft.

d) Group IV: All the failures of Group I undergoing revision using tragal composite cartilage graft only.

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Surgery was performed by Registrar and consultant grade surgeons. Temporalis fascia was used in 23 ears and tragal cartilage perichondrium autograft in rest 23 ears. The opeative procedure was standardized for both groups of patients. The ear was first prepared by shaving the adjacent scalp. The pinna, post aural skin and meatus were than cleaned using Betadine solution. The patient was draped and the postaural skin and meatus were infilterated with 2% lignocaine and 1/200,000 adrenaline. Following freshening of the perforation edges, a posteorinferior tympanomeatal flap was elevated. The drum was grafted with an underlay temporalis fascia or tragal composite cartilage graft on a gelfoam bed depending upon the group of patients. Small pellets of gelform soaked in antibiotic solution were placed over the graft and the ear canal.Tympanic membrane perforation repair was carried out by the following methods:-

a) In small and large perforation composite graft was fashioned to cover the defect with the bare surface of cartilage facing the middle ear and part of perichondrium reflected on to the canal wall.

b) In attic retraction pocket and Marginal perforation the perichondrium composite cartilage was fashioned to cover the drum defect area and to reconstruct the posterior bony canal wall and or scutum after adequate inspection of middle ear and ossicular integrity.

c) In total perforation the annulus was fashioned using circumferential cartilage batten attached to one surface of a perichondrial autograft.

In each case the external auditory canal was packed using gauge soaked in povidine iodine aural pack was removed after seven days after removal of sutures. The measurements of pre-operative and post-operative air-bone conduction thresholds over the speech frequencies (500, 1000 and 2000 HZ), served to calculate the post-operative air-bone gap closure. Suture were removed after seven day and patients were followed up after one, three, six and 12 months for anatomical restoration.

Observation and Results:

In our study of forty six ears which were taken up only type I tympanoplasty, thirty seven ears (79%) were successful (table I). Out of nine ears (21%) which failed, three showed avasculr necrois of graft within one month, four ears developed innfection leading to central perforation and two ears had anterior defects.

Table-I: Overall Results - Tympanoplasty (Type-I)

	Success	Failure	Total
Number of Cases	37	9	46
Percentage	79%	21%	100%

Tympanoplasty using temporal fascia was successful in seventeen ears (74%), while tympanoplasty using tragal perichondrium cartilage composite graft was successful in twenty cases (91%) (Table II & III).

Table-II: Tympanoplasty using Temporal Fascia

	Success	Failure	Total
Number of Cases	17	6	23
Percentage	74%	26%	100%

Table-III: Tympanoplasty using tragal prichondrium composite Graft

	Success	Failure	Total
Number of Cases	20	3	23
Percentage	91%	9%	100%

Reconstruction of posterior canal wall and scutum was performed in ears with retraction pockets and posterior marginal perforation, an overall success rate of 70% (Table IV). In 5 ears scutum was recostructed, it was successful in 4 ears(80%) Posterior canal wall was reconstructed in 5 ears out of which 3 ears (60%) were successful (Table V). The cause of failure was postoperative infection.

Table-IV:
Tympanomastoid Reconstruction

	Reconstruction of Scutum Using Composite Cartilage		Reconstruction of Posterior Canal Wall	
	No. of Cases	% Age	No. of Cases	%age
Successful	4	80	3	60
Unsuccessful	1	20	2	40
Total	**5**	**100**	**5**	**100**

Postoperative audiometry after twelve months showed that in cases where temporalis fascia was used three cases (12%) had improvement in air coduction threshold by 10 db, nine ears (39%) achieved greater than 20 db improvement in (air-bone) gap.

In cases where composite cartilage graft was used four (18%) ears achieved 10db improvemet, nine ears (39%) achieved 10-20 db improvemet and rest seven ears (36%) achieved more than 20db improvement in (air-bone) gap (Table V). Six ears in which temporal fascia graft failed to take up, revision tympanoplasty was performed using tragal perichodrium cartilage composite autograft only. All these cases were successful (Table VI). Out of six revision tympanoplasty cases, for ears (66%) showed 10-20 db improvement in air-bone gap and rest two ears (33%) improved 10 db (Table VII).

Table-V: Improvement in hearing in post operative period in successful cases

Type of Graft	No. of cases	Gain in db	Percentage
Temporalis Fascia (17 out of 23)	3	0-10	12
	9	10-20	39
	3	> 20	12
Perichodrium Cartilage composite Graft (20 out of 23)	4	0-10	18
	9	10-20	39
	7	>20	36

Table-VI: Revision Tympanoplasty (Composite Graft)

	Success	Failure	Total
Number of cases	6	0	6
Percentage	100	0	100

Table-VII: Improvement in hearing in postop-Period in Revision cases

No. of cases	Gain in db	Percentage
2	0-10	33%
4	10-20	66%

Discussion:

The term tympanoplasty was used to describe surgical reconstructions of the middle ear hearing mechanisms that has been impaired or destroyed by suppurative disease (Wullstein, 1953). The operating microscope, first applied to these operations by Wullstein & Zoller, has become indispensable for this type surgery. To date most widely graftig material is temporalis fascia. Since then number of procedures have been tried using various modes of reconstruction.

Goodhill (1967) and Adkins (1990) observed that normal tissue of the TM possesses a powerful regenerative capacity due to:

(i) The induction effect of fibrous annuals.

(ii) A special nature of basement membranelaminae in the middle layer of the TM. Based on the conviction that donor mesodermal tissue in close prosimity to the recepient area provide the most physiologically desirable autograft the use of perichondrium cartilage graft for reconstruction of the tympanic membrane, scutum and posterior canal wall was popularised by Mcleive (1969) similarly we used the tragal perichondrium composite graft & compared it to temporallis fascia graft. The perichondrium cartilage graft has excellant contour, survival capacity and freedom from osteogenic or chondrogenic tendencies (Goodhill, 1969). These properties enable these grafts to withstand poor vascularity and thus have a higher take rate as compared to temporal fascia as seen in our series (Table No. II & III).

The stiffness and contour of perichondrium cartilage graft prevents anterior blunting and resists resorption and retraction (Dorn hoffer,1997). The contour and stiffness of perichondrium cartilage graft also helps in functional improvement by better conduction of sound stimulus as seen in our series. In perichondrium cartilage composite graft group, hearing improvement in (air-bone) gap closure is better compared to temporalis fascia graft which is similar to a study conducted by Mukherjee & Chamyal (1997). This study concluded that:-

1. Tragal perichondrium composite graft enjoyed better take rate over temporalis fascia.
2. Higher take rates are ascribed to excellent contour and lower biogenicity to withstand poor vascular conditions.
3. The gain in hearing were better in composite cartilage graft compared to temporalis fascia.
4. The texture and contour of perichondrium cartilage graft helps in achieving near normal physiological and anatomical condition.
5. Cartilage perichondrium composite autograft is the material of choice for revision tympanoplasty.
6. Composite cartilage perichondrium better graft helps in reconstruction of scutum & posterior canal wall & in total perforation the cartilage forms the circumferential support.
7. Longterm follow up is required to assess efficacy of tragal composite cartilage autograft for retraction pockets.

Therefore this study demonstrates that composites cartilage tympanoplasty offers the possibility of a rigourous TM reconstruction.

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NEONATAL CHOLESTASIS IN KASHMIRI CHILDREN

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Abstract: *Neonatal cholestasis is prolonged elevation of conjugated serum Bilirubin (more than 20% of total bilirubin) beyond first fourteen days of life[1]. After extensive evaluation a diagnosis of either Biliary Atresia or Neonatal Hepatitis (NNH) is made in 70% 80% of cases[2] Neonatal hepatitis and biliary artesia form a pathophysiologic process directed at various levels of the hepatobiliary tract. Inflammation in the bile duct epithelium may result in the sclerosis and obliteration of the bile ducts and manifest as biliary atresia. Primary hepatocellular inflammation is more likely to result in neonatal hepatitis. One half cases of neonatal hepatitis resolve without sequelae, while most of the biliary atresia cases require surgical intervention for repair or ultimately liver transplant[3].*

Key words: *Cholestasis, Biliary atresia, Neonatal hepatitis, Liver Biopsy.*

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Material and Methods:

This prospective study was carried out in the Department of Neonatology and Critical Pediatrics at Sher-e-Kashmir Institute of Medical Sciences, Srinagar, which is a tertiary care university hospital. Out of 12000 admissions from June, 1997 to June, 1999, 256 cases had jaundice and out of these 40 patients had cholestasis. Patients were evaluated clinically and hemogram, liver function tests, urine and blood cultures, coagulogram, kidney function tests, HBs Antigen, Thyroid function test, abdominal ultrasonography (USG), hepatobiliary nuclear scan (99m Technicium labelled Mebrofenin) and liver biopsy were done. Live biopsies were done with disposable tru-cut (Travenol Labs, USA) needles.

Presence of intrahepatic biliary radicle dilatation, absece of gall bladder and absence of dilatation of the bile duct at hilum were considered suggestive of biliary atresia at ultrasono-graphy.Presence of normal gall bladder and common bile duct at USG were considered favouring neonatal hepatitis[4]. At scintigraphy, absence of radioactivity in the small bowel at 24 hours was taken as indictive of biliary atresia. The presence of radioactivity in small bowel within 6 hours was considered diagnostic of neonatal hepatitis[5]. Standard criteria were used for the diagnosis of biliary atresia (enlarged portal tracts, bile ductular prolifera tion, portal tract fibrosis and bile plugs in portal triads), Neoatal hepatitis, collection of mononuclear cells,in the hepatic lobule, fatty changes in the hepatocytes uneven staining of hepatocytes and predominant giant cell transformation and the paucity of intra-lobular bile duct (PILBD) on liver histology[6].

Results:

Out of 1200 admissions over period of two years, 256(21.3%) cases had jaundice 40 patients (3.3% our of total admission and 15.6% out of jaundice cases) were diagnosed as cholestasis (conjugated bilirubin more than 20% out of total bilirubin) 25 patients (62.5%) female Age group was between one month to 6 months.

Liver function tests were deranged in all the patients. Serum bilirubin was more than 15 mg in 20 (50%) cases, 5-15mg in 10(25%) and less than 5 mg in 10 cases (25%) Alkaline phosphatase and SGPT was increased in the all the patients. Blood cultures were positive in 8 patients (20%) with Klebsiela and E. coli in 3 patients each & pseudomonas in two patients. Urine cultures were sterile in all the patients. HBs Antigen was positive in 4 (10%) patients TORCH screen revealed 4 (10%) patients as Toxoplasmosis positive. Thyroid function tests were normal in all cases. Coagulogram was deranged in 10 (25%) cases, for which inj. vit-K 5 mg x oD for 3 days was used in addition to given fresh forzen plasma before going for liver biopsy (Table 1).

Abdominal ultrasonography (USG) gives definitive diagnosis of choledochal cyst. Ultrasonography has an accuracy of 80% in differentiating Neonatal hepatitis from Biliary atresia, visualisation of gall bladder while fasting(4 hours) which contracts normally on feeding virtually rules out Biliary artesia[7]. The reverse is not always true and in neonatal hepatitis the gall bladder may or may not contract on feeding. In our study no patient was diagnosed as having choledochal cyst. Gall bladder was visualised in 25 (62.5%) cases and a post

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feed contraction was. seen in 20 (50%) patients.

Table-I

Total No. of Cases	(n 40)	%age
Biliary Atresia	15	37.5
Neonatal Hepatitis	25	62.5
Blood Culture Positve	8	20
HBS Antigen Positive	4	110
Toxoplasmosis Positive	4	10
Idiopathic	9	22.5

In radionuclide scanning using the latest Technecium 99m labelled iminodiacetic acid (IDA) - Mebrofenin which has low renal excretion, high hepatic uptake and rapid biliary excretion[8] 25 patients (62.5%) showed some activity in the intestines in early or delayed pictures whereas 15 cases (37.5%) showed no excretion of the traces in any scan pictures.

Liver biopsy has a differenciating accurary of 83.97% in Biliary Astresia andNeoatal Hepatitis. The predominant features in Biliary Artesia are involvemet of portal tracts (widening of portal tracts, bile duct reduplication, portal fibrosis) whereas Neonatal Hepatitis demonstrates hepatocellular disease (ballooning necrosis, giant cells, inflammation). In our study liver biopsy favoured a diagnosis of Neonatal Hepatitis in 25(62.5%) cases and Biliary Atresia in 15(37.5%) cases (TableII).

Table-II

Total No.of Cases:-	(n40)	%age
Ultrasonography (USG) findings:-		
- Gall bladder visualised	25	62.5
- Gall bladder not visualised	15	37.5
Radionuclide Scan:-		
- Neonatal Hepatitis	25	62.5
- Biliary Atresia	15	37.5
Liver Biopsy Fินidings:-		
- Neonatal Hepatitis	25	62.5
- Biliary Atresia	15	37.5

Discussion:

In our study presentation of patients was in the age group of 1-6 months, whcih is similar as with other studies[9,10]. In our study 15.6% cases had cholestasis, which is slightly less as compared to 19% with other[9]. Neonatal hepatitis was found in 25 (62.5%) cases and biliary atresia in 15(37.5%) cases in our study compared to 23% and 77% in other studies[9,10] respectively. Blood cultures were positive in 8(20%) and HBs Antigen positive 4(10%) cases. None of our patients had urine culture positive, nor was any patient having hypothroidism, syphilis, Cytomegalovirus; herpes or rubella infection. None of these patients received total parental nutrition and malaria is not seen in this part of country.

Abdominal USG, Nuclear Scan and Liver Biopsy in combination made us to get the diagnosis of Intrahepatic Biliary Atresia in 15(37.5%) and Neonatal Hepatitis in 25(62.5%) cases. This is in comparison to more cases of Biliary Atresia and lesser number of Neonatal Hepatitis seen by others[9,10]. Ten patients of Biliary Atresia, out of 15 total, have succumbed to terminal liver disease and5 are being managed as cirrhosis. Out of 25 cases of Neonatal Hepatitis, 15 are doing well, 5 are under follow up as cirrhosis and 5 patients were lost in the follow up.

Neonatal Cholestasis, a fairly common liver disease in children, presents either in the neonatal or post-neonatal period. The outcome for Neonatal Hepatitis is good whileas it is gloomy for the Biliary Atresia, except for choledochal cyst. The reasons for this being late referrals of such patients, usually in the post-neonatal period and the surgical expertise not available at all the places. Outcome after the Kasai procedure also is not very good and liver transplantation may be the ultimate answer. Role of other factors remains undermined yet dietary toxins consumed by mother and some other viruses may be responsible for neonatal cholestasis syndrome as more and more needs to be explored for this liver disease in children.

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PRIMARY AND SECONDARY COMMON BILE DUCT STONES, COMPARATIVE CHEMICAL ANALYSIS

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ABSTRACT: The present study consists of comparative chemical analysis and bacteriological study of two groups of common bile duct stones (primary & secondary) with each group consisting of 25 patients.

Analysis revealed that secondary duct stones had more of cholesterol and less of calcium and bile pigment, while primary duct stones had more of calcium and bile pigment. E.coli was the commonest organism grown from cultures. Infection was associated in both types especially in primary duct stones. It seems that infection appears to be responsible for common bile duct stones predominantly those of primary type.

Key words:

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INTRODUCTION

Gallstones disease is afflicting a fairly significant human population throughout the world with a wide variation from region to region. In Pima Indians of North America 70% of women have gall stones by the age of 30 years while same percentage of men get it by the age of 60 years[1]. On the other hand Masai tribe of east Africa are free from gall stones disease[2]. The variety of composition difference in gall stones from cholesterol to the pigment reflects the different mechanisms and etiological factors in there formation which remains obscure and as such no prophylactic measures to cure it. Amongest other studies one of the first step to know the exact cause of stone formation is the chemical analysis of stones from the biliary tree. Although gall stones may be silent or cause pain or fatty dyspepsia, common duct stones can cause obstruction leading to cholangitis, thus an important cause of morbidity and mortality. As such the treatment of common duct stones is a priority one and should not be delayed.

Stones may form in gall bladder and slip into common bile duct (secondary stones) or form itself in the biliary duct system in a normal gall bladder or in patients who have already got gall bladder removed. The pathology in secondary stones is attributed to an abnormal bile and gall bladder stones which precipitates stone formation, while as primary stones are purely due to an abnormal lithogine bile or infection. In order to understand the chemical difference between the primary and secondary bile duct stones, this study was undertaken.

MATERIAL AND METHODS

This study was conducted on fifty patients who were admitted for surgery having biliary stone disease. The age group ranged from 20-50 years. Out of 50 patients 36 were female and 14 were males. Twenty five patients had common duct stones alongwith gall stones which were labelled as secondary stones. These were compared to 25 patients who had stones in common bile duct with normal gall bladders.

Before exploration of the common bile duct, using a 24 G needle 5ml of bile was aspirated from it. This was sent for bacteriological examination. Stones were removed through choledochotomy, washed with normal saline and sent to laboratory for analysis of various chemical constituents by the method of stepwise solvent extraction (modified method of Holt and Tronky)[3].

RESULTS

Cholesterol was found in greater amount in secondary duct stones as compared to primary duct stones, while as bilirubin was higher in primary stones. Calcium was significantly more in primary stones but phosphate and proteins were nearly in equal amounts(Table I).

The amount of residue in both types of stones was not significantly much different. Residue is considered to be the organic matrix shell on which the constituents get deposited. It is usually mucopolysaccharides and mucus substances.

Bile cultures revealed growth of bacteria in both groups of patients (Table II). E. coli was the commonest organism grown followed by klebsiella, streptococcus and staphylococcus. E. coli was positive in 75% of cultures in primary duct stones.

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DISCUSSION

Although gall bladder was previously thought to be the primary site of stone formation and common duct stones were slipped stones, but it has been proved beyond doubt that stones can form de-novo in hepatic ducts or common bile duct in presence of a normal gall bladder or in those patients in whom gall bladders have been already removed and as such designated as primary duct stones[4,5]. The presence of primary duct stones indicate a basic altered pathophysiology of bile rather than gall bladder to be responsible for stones formation. On the other hand in a number of patients who have gall bladders packed with stones, have completely free normal bile duct system, indicating that gall bladder formation also pay important role in gall stone formation along with abnormal bile composition.

Table I. Chemical composition of common duct stones

	Constituent mg%	Primary stones Range	Mean	Secondary stones Range	Mean
1.	Cholesterol	29.0-96.0	74.5±16.2	12.0-57.0	40.8±5.1
2.	Bilirubin	5.2-23.1	18.2±5.2	8.1-30.0	27.2±1.7
3.	Calcium	1.9-10.1	7.3±2.6	2.1-18.6	13.1±4.3
4.	Phosphate	0.2-6.3	4.1±3.1	0.8-5.2	3.9±4.1
5.	Proteins	0.1-5.2	3.2±1.2	0.5-2.3	2.0±1.1
6.	Residue	0.4-41.1	18.1±12.3	0.9-33.5	20.2±6.7

Stones orgniating in gall bladder are likely to contain a large proportion of cholesterol, while stones developing within the bile ducts consist more of bilirubin and calcium salts. However, the relative amount of bilirubin, cholesterol, calcium and other compounds that these stones may contain depend upon existing circumstances[6]. Thus ethnic and geographic factors, presence or absence of hemolysis, relating concentration of cholesterol, bile salts and lecithin in the bile secreted by liver and nature of any associated inflammatory changes in the living cells of the bile ducts, the degree of biliary obstruction and the presence of bacterial infection, all influence and help in particularizing the chemical composition of duct stones[7]. Ductal inflammation and bacterial contamination commonly accompany choledocholithiasis and also form the important etiological factors for primary duct stones[8]. Maki found increased bacterial b-glucouronidase activity in bile harbouring bile pigment stones. Hydrolysis of bilirubin glucouronide and coupling of free bilirubin with calcium may lead to bile pigment stone formation[9].

Table II: Bile culture in common duct stone

	Organism grown	Secondary stones No	%	Primary stones No	%
1.	Sterile	8	32	3	12
2.	E. coli	11	44	18	72
3	Klebsiella	3	12	2	8
4.	Staphylococcus	2	8	1	4
5.	Streptococcus	1	4	1	4

Bacteria are also known to produce lipase and phospholipase which split phospholipids, thus disturbing cholesterol phospholipid ratio and causing precipitation of cholesterol[9]. The presence of calcium and pigment in primary common duct stones signifies the role of infection alongwith altered biliary composition. Under normal conditions, the sphincter of Oddi forms an effective barrier to ascending bacterial migration and free flowing bile also inhibits colonization[10]. However Sung et al showed in cats that it is possible for bacteria to invade the biliary tract through the portal venous system and that transient bacteriobilie occurs[11,12]. Gall bladder appears to be the organ responsible predominantly for cholesterol stones and secondary common duct stones which originally develop from gall bladder and later in common bile duct.

Wosiwitz[13] suggested the possibility of secretion of b-glucouronidase by ductal epithelium, a lower bile salt concentration in common duct bile, (which would result in less colloidal stability and less binding of calcium) and higher pH of common bile duct. In patients with common duct stones, excess mucus secretion from the duct epithelium forms poultices masses which engulf the pigment, calcium and cholesterol forming biliary concentrations.

Some form of obstruction or stasis is necessary to be present for development of common duct stones which may include sphincter of oddi dysfunction or stasis due to mucus masses[13]. Stasis thus present provides favourable circumstances for proliferation of bacteria in the biliary tree.

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MYTH BREAKER ABOUT SURGICAL FACE MASK

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Abstract: Use of surgical face masks which is so rigidly followed in our operation theatres has never been found to be beneficial to the patient, however benefits tothe surgical team cannot be ruled out. A study was conducted over a period of 32 weeks involving 921 operations. After 460 operations performed using face masks. 26 wound infections occured accounting for a percentage of 5.6%. After 461 operations performed without using surgical face masks 23 infections occured accounting for percentage of 4.9%. Besides, no significant differences in nature of bacterial cultures obtained from two groups was seen. So need for re-evaluating use of surgical face masks is there.

Key words: Surgical face masks, Wound infections, Culture.

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Introduction

Since last hundred years surgical face masks have been an intimate component of aseptic surgical technique, but only a few workers questioned as to how much important it was to wear a surgical face mask. It was Mikuliez[1] in 1897, who first mentioned the use of surgical face mask. Later on Flugge[2] demonstrated presence of bacteria in droplets in the nose and mouth and this further strengthened the logic of using surgical masks. Then began an array of different types of surgical face masks being used with all of them focussing on their ability to filter particulate matter. Ritter and associates[3] found 33 fold increase in counts of airborne bacteria when 5 persons entered an empty operating room but there was no difference in whether masks were worn or not. It was in 1981 that Orr[4] worked on influence of face masks on role of surgical wound infections. In his study Orr did 1049 procedures and all rountines remained unchanged except that nobody wore a mask. Eight persons were infected at a rate of 1.8%, a rate significantly lower than that experienced during the four preceeding years. Besides, the infections which occured bore no relation to the throat or nose cultures from the members of surgical team. Later Rithman and Colleages[5] did a study of infection rates after suture oflaceration wounds in an emergency department, they found no difference in regard to whether cap and mask were used or not. Then Lett and Doerner put forward an hypothesis to explain the reduction of post operative wound infections by omitting the masks as found by Orr. As per this hypothesis, face masks by friction release skin scales carrying bacteria, most often staphylococci from faces of surgical team. This friction can be avoided by omitting the mask. Instead of getting contaminated by pathologic skin streptococci the wound would be contaminated by an increased number of L streptococci, not known to cause wound infection in general surgery[6,7]. Tuneval then did a prospective study in 1991[8] in which he performed 1537 operations with face masks, 73 infections were reported at a rate of 4.7%; for 1551 operations performed without masks 55 infections occurred at a rate of 3.5%. Besides bacterial species cultured from wound infections did not differ in any way. On these findings Beck[9] suggested that the mask be replaced by splash-shield, whose function is to protect surgeon from the hazards associated with transmission of blood borne pathogens.

Material and Methods

A study was done to evaluate the above mentioned findings of various workers. In this study various surgeries were done with face masks and many without it. In all 460 surgeries were done with face masks and other 461 without using them. Then rate of wound infections was calculated in each group. Then cultures were taken from infected wounds and subjected to study of organisms. The whole study was conducted over a period of 8 months.

Results

In all, a total of 49 wound infections occurred in 921 cases operated accounting for 5.35 age of wound infection out of this 26 cases of wound infections occurred among 460 cases in masked group (5.6%) and 21 cases occurred among 461cases in unmasked group (4.9%).

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S. No.	Surgery	With face masks Surgeries performed	With face masks Wound Infections	Without face masks Surgeries performed	Without face masks Wound Infections
1.	Appendicectomies	139	11	125	10
2.	Resection anstomosis of small gut	56	5	40	3
3.	Splenectomies	4	0	5	1
4.	Exploratory laparotomies (without ressection)	20	2	40	3
5.	Hernias (Ingurial)	58	3	60	1
6.	New phrectomies	64	3	82	4
7.	TURP	25	0	20	0
8.	Pyelolithotomies	95	2	89	1
	Total	**460**	**26**	**461**	**23**

Bacterial cultures taken from wound infections were taken which revealed following findings:

S.N.	Infections	With face masks Single	With face masks Mixed	Without face masks Single	Without face masks Mixed
1.	Staphylococous aureus	4	3	2	4
2.	Staphylococus epidermid's	1	3	1	2
3.	Pyogenic s streptococcus	1	-	-	1
4.	Streptococus Viridans	1	-	-	-
5.	Escherichia coli	-	12	1	11
6.	Other aerobes gram negative	1	10	1	9
7.	Bacterioids	-	8	4	10
8.	Anaerobic gram positive cocci	-	2	-	4
9.	Pseudomonas	-	1	-	-
10.	No culture	-	2	3	-
11.	No growth	-	1	-	1

Whether after masked or unmasked operations, results of culture are placed separately in two headings single or mixed, depending on number of bacterial strains found. Staphylococci were found in 7 cultures after operations without face masks and in 7 cultures with face masks. Since there were 5 cultures in which no growth could be obtained so only 42 cultures were to be evaluated. So rate of staphylococcial infections without face masks is 1.5% and lwith face mask is 1.95%. This difference is not statistically significant. Incidence of infection of other organisms can be similarly compared.

Discussion:

Since last century there has been an advance in all aspects of patient care so pertinent infections in clean surgical wounds is infrequent in most centres today. If wound infection occurs it increases duration of stay in the hospital, morbidity and cost of treatment. So prevention of wound infection is one of the major goals for surgeons. In this direction, many practices are in vogue,all aiming at aseptic surgery, many of them are in practice because of the fact that our seniors have been doing them and one of them is use of surgical masks. Their beneficial effects to the patients have never been documented scientifically and if documented they have not stood the test of the time. Despite this fact, masks have been found to have protective role for operating team from drops of blood, which might be infected with Hepatitis B virus or HIV. It might also protect the staff from airborne infections from patients.

Besides medical facts, there is one more important consideration and that is increasing cost of medical services and by stopping use of surgical face masks cost of surgery may decrease to some extent. If there are seven people in operating team (including anesthetists and nurses) and everybody wears a mask, then cost of wearing masks means Rs. 140.00 per surgery (if cost of one mask is Rs. 20.00). Now it is a matter of whether we are ready to go against our ritual practice or not?

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COMPARISON BETWEEN THE EFFECT OF ATROPINE AND GLYCOPYRROLATE ON GASTRIC FLUID VOLUME AND ITS PH IN PARTURIENTS

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Abstract: The effect of premedication with anticholinergic agents, atropine and glycopyrrolate on gastric juice pH and volume, given one hour before induction of general anesthesia to patients about to undergo caesarean section, was investigated. Stomach contents were retrieved and the volume and pH measured. Results were compared to control group of 50 non-premedicated parturients. The effect of glycopyrrolate premedication on gastric juice pH and volume was significant.

Key words: Premedication,Atropine, Glycopyrrolate, Obstetric anesthesia.

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Introduction:

In pregnancy, the production of gastrin, the hormone that increases both acidity and volume of gastric contents, is increased. Motilin, a hormone that speeds gastric emptying is depressed during pregnacy and labor[1]. Gastric emptying is slowed also due to displacement of pylorus by gravid uterus, increased levels of progesterone, pain and anxiety. All these changes increase the risk of regurgitation and aspiration pneumonitis during general anesthesia. Atropine and glycopyrrolate are administered as pre-anesthetic medication for antisialic and vagolytic effects to reduce volume and acidity of stomach contents pre-operatively. The studies comparing the effects of anticholinergic drugs like atropine and glycopyrrolate on gastric volume and its pH in parturients are few and not clear[3]. The present study was undertaken to assess these effects of anticholinergics when given intramuscularly as pre-anesthetic medication in usual clinical doses.

Patients and Methods

The investigation was undertaken in 150 patients of physical status ASA-Ior II scheduled for elective caesarean section under general anesthesia. Patients were allocated randomly to three groups. In the control group (Group I), no premedication was given. Group II patients received atropine sulphate 0.6mg intramuscularly 60 minutes before induction and Group III patients received glycopyrrolate bromide 0.2mg intramuscularly 60 minutes before induction as premedication. All patients fasted overnight.

Anesthetic induction was accomplished with I.V. injection of sodium thiopentone, 5mg/Kg followed by succinylcholine. This was followed by tracheal intubation with a cuffed tube. 16 French nasogastric tube was inserted in the stomach. Gastric contents were aspirated for pH and volume determination. Data were analyzed using students 't' test. $p<.05$ was considered significant.

Results

Patient' age and weight werer similar in the three groups (Table-I)

Premedication grop	Number	Age (years) Mean±SD	Range	Body weight (Kg) Mean±SD	Range
Control	50	27.40±2.34	22-32	56.22±4.35	48-68
Atropine	50	27.84±4.42	19-36	53.40±5.50	44-70
Glycopyrrolate	50	28.70±3.92	21-37	54.22±4.52	45-65

Table-II: Gastric Volume and Acidity Measurements

Premedication group	Number	Volume of gastric contents(ml) Mean±SD	p	pH Mean±SD	p
Control	50	26.98±6.21	-	2.13±0.16	-
Atropine	50	26.82±11.10	<0.001*	2.11±0.13	<0.001*
Glycopyrrolate	50	10.82±9.32	<0.001**	4.46±0.44	<0.001**

**P<.001 when G-II compared with G-III.*

***P<.001 when G-I compared with G-III.*

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Table-III: Gastric Fluid pH Elevation and Volume Depletion (Percent)

Premedication group	pH	Volume (ml)
Control	42.0	26.0
Atropine	39.7	41.39
Glycopyrrolate	195.36	73.65

The non-premedicated control group had an average gastric volume of 26ml and mean pH was 2.13. Patients premedicated with atropine showed little difference from the control group ($p>.05$). Glycopyrrolate was effective in increasing gastric fluid pH and decreasing gastric volume ($p<0.001$).

The average volume was 10.82 ml ($p<0.001$) (Table-II &III).

Discussion

The anticholinergic drugs as premedication before anesthesia have been used in an attempt to increase pH and reduce volume of gastric contents[7]. Acid aspiraton pneumonitis is most likely when the pH of the aspirated fluid is below 2.5 and volume exceeds 0.4ml/Kg[1,8].

The present investigation has shown that premedicating the patient with atropine does not significantly increase the gastric juice pH to safe levels, while premedicating with glycopyrrolate can raise the pH above the critical level of 2.5. Safety is further significantly increased when the premedicatioin - induction time is prolonged to 60 minutes[3]. Salem et al (1976)[3] observed significant suppression of gastric acidity with glycopyrrolate than atropine. Black and Watson (1978) showed that effects of glycopyrrolate on gastric acidity are equivocal. These differences in published data are difficult to explain but may be related to differences in patients studied[4]. The overall pH elevation was 40 percent with atropine and 195 percent with glycopyrrolate when compared with control group (Table-III).

It was not possible to determine whether the stomach was completely emptied by the gastric tube placed in our patients. Therefore, the measured gastric fluid volumes may have understimated the true volumes. Nevertheless, using the guidelines of a gastric fluid volume below 0.4ml/Kg the present data suggest that patients premedicated with atropine and glycopyrrolate had average gastric volumes of 26ml and 11ml respectively ($p<0.001$). Besides it, reduction in voluume was 41 percent and 73 percent, when compared to control. Young and Sun (1962) observed that glycopyrrolate reduces the gastric volume significantly[5]. Baraka et al (1977)[3] also observed the same effects with glycopyrrolate and atropine.

Although both atropine and glycopyrrolate in the present study reduced the gastric volume below critical level of 0.4m/Kg, glycopyrrolate was more effective in elevation of pH and reducing volume ($p<0.001$).

Glycopyrrolate possesses other advantage in obstetric anesthesia. Because it is a quaternary ammonium compound, it is highly lipophobic and penetrates with difficulty through lipid membranes such as blood brain and placental barriers. Heyman et al (1976)[6] showed that glycopyrrolate have no significant effect on fetal heart rate, whereas the administration of atropine produced a significant increase in fetal heart rate.

In conclusion, we have shown that glycopyrrolate premedication raises the pH of gastric juice above the critical levels of 2.5 and reduced gastric fluid volume in most of the patients. Safety to fetus and longer duration of action also make it a preferred agent for use in obstetric anesthesia.

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PRIMARY TUBERCULOSIS OF STOMACH: A CASE REPORT

Arun Kumar Gupta M.S.; P.C. Sood M.S.; B.B. Sharma M.D.; S.S. Minhas M.S.; Pamposh Raina

Introduction

Tuberculosis of stomach is a rare entity and is usually secondary to a tuberculous lesion elsewhere[1,2]. Primary gastric tuberculosis is extremely rare[3,4]. The clinical, radiographic and endoscopic findings of gastric tuberculosis are likely to be confused with gastric neoplasm[3-6]. The diagnosis is confirmed by histological examination[7]. We are reporting a case of primary gastric tuberculosis simulating gastric carcinoma.

Case Report

Mr. S.K., aged 36 years, was admitted in Indira Gandhi Medical College, Shimla on 7-8-98 with complaints of upper abdominal pain and loss of weight for six months and vomiting for 20 days. The patient had lost 8 kg of weight in last six months. The chest was clear clinically and there was no palpable peripheral lymphadenopathy. Chest skiagram was normal. Barium meal examination showed a filling defect in the pyloric region of stomach. Upper gastrointestinal endoscopy revealed irregular ulcer and nodularity on lesser curvature of stomach in pyloric region. Diagnosis of carcinoma of pyloric end of stomach was made and a laparotomy was performed on 21—8-98. The laparotomy revealed a hard mass in pyloric region of stomach with enlargement of paragastric lymph nodes. Distal radical gastrectomy with Billroth-II recostruction was performed. The histopathological examination of the resected tissue showed lymphoid follicles, areas of caseous necrosis, epitheloid cell granulomas and langhan giant cells. The resected paragastric lymph nodes showed caseous graulomas. The patient was put on antitubercular therapy. The post operative course was uneventful without any evidence of complications or relapse. The patient was well and gaining weight when seen six months after surgery and was still on antitubercular treatment.

Discussion

The stomach is comparatively a rare site for the development of tuberculosis. The incidence of gastric tuberculosis is 0.20 to 0.22 percent[2]. Most of the gastric tuberculosis cases reported previously were secondary to other tuberculous lesions[1,2]. Half of these gastric tuberculosis cases had pulmonary tuberculosis, the other half were secondary to tuberculous lesions in the other organs e.g., kidneys, liver, lymph node, intestine[8,9]. Only a few cases of primary gastric tuberculosis have been reported in literature[3,4]. In their review of the cases, Misra et al found only 4 cases of primary gastric tuberculosis reported until 1980[4]. The rare occurrence of gastric tuberculosis may be due to effect of gastric acidity on tubercle bacilli, relative paucity of lymphatics in stomach, barrier of the gastric mucosa and rapid emptying of stomach[1].

Gastric tuberculosis usually affects young patients. It commonly presents with peptic ulcer like picture i.e. abdominal pain, vomiting, gastric outlet obstruction and gastrointestinal bleeding[1-3,8]. There is no pathognomonic picture of gastric tuberculosis on either barium meal oor endoscopy[5,6]. The only way to diagnose gastric tuberculosis is by histological and bacteriological confirmation. The lesser curvature of the antrum and prepylorus are the most common sites of the tuberculosis lesions[3-6,9]. Single or multiple irregular ulcerated lesions are most commonly seen surrounded with inflammed and necrotic tissue[9]. The second commonest appearance is in the form of hypertrophic infilterative lesion[8,9]. Pyloric stenosis may be primary to hypertrophic infiltrative lesion itself or secondary to inflammatory reaction or fibrosis. Microscopic examination often reveals the typical caseating granulomas located in the mucosa and submucosa but rarely extending to the muscular layer[1,9]. Because of lack of accurate clinical, radiological or endoscopic diagnosis, most cases of gastric tuberculosis are diagnosed as carcinoma of stomach ad gastrectomy is done[2]. The diagnosis is made by histological examination after surgery[1,2,7].

Treatment of gastric tuberculosis is by atitubercular drugs and all patients are expected to respond to medical treatment[1,10]. The surgical intervention is necessary in most of the chronic gastric lesions especially with gastric outlet obstruction. Surgery may be useful adjunct to chemotherapy where a large caseous lesions hinders penetration of drugs in to the lesions[10].

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Summary

A case of primary gastric tuberculosis in a 36 years old male is reported with review of literature. Surgical resection was done and post perative antitubercular chemotheraphy was given with satisfactory recovery.

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NEUROCYSTICERCOSIS - PRESENTING WITH CONVULSION IN A KASHMIRI MUSLIM

G.Q. Khan M.D.; G. Hassan, M.B.B.S.; M. Yaseen M.D.; S. Qureshi M.D.; W. Qureshi M.B.B.S.; Iftikhar M.B.B.S.

***Abstract:** Neurocysticercosis is not found in Muslims because of religious prohibition of intake of pork.A 65 year old Kashmiri muslim presented with seizures and was diagnosed as a case of Neurocysticercosis and treated with albendazole.*

***Key words:** Neurocysticercosis, Convulsions.*

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Case Report:

A 60 years old Kashmiri muslim was admitted with complaints of recurrent generalized tonic colonic seizures for 2 months. There was no history of headache, vomiting, weakess of any part of body, change in behaviour, visual impairment, nasal regurgitation, or change in speech. No history of taking pork. He had been doing business for more than 20 years outside the state. There was no history of hypertension or diabeties mellitus. General physical examination and systemic examination was normal. His neurological examination was normal. Ophthalmological examination including fundus was normal. He was evaluated for late onset seizure disorder.

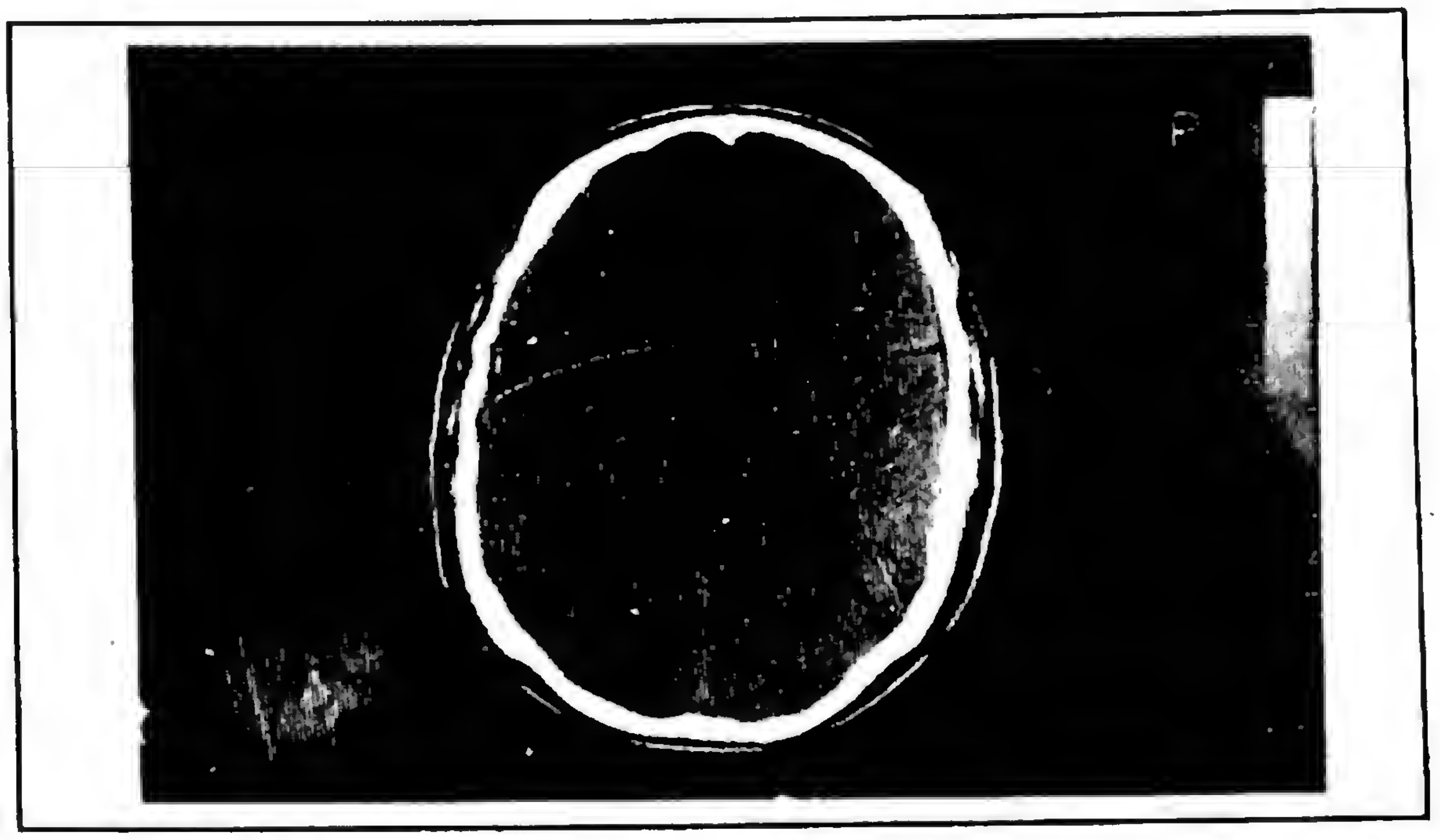
Investigation:

Haemogram, urine examination L.F.T. kidney function tests, Electrolytes, Blood sugar, X-ray chest (PA view). USG abdomen, E.C.G., x-ray skull AP/Lat. were normal. CT scan showed two cystic lesions in cerebral cortex, one each in frontal and occiptal lobes, radiological opinion was that of neurocysticerocosis[1]. Casoni's text and hydatid serology was negative tuberculin test negative. IHA (cysticerosis) was positive, CSF examination was normal. So he was diagnosed as a case of Neurocysticercosis.

Patient was put on Albendozole 400 mg TID for 2 weeks plus anticonvulsants (phenytoin 100mg TID). He improved, and is seizure free for the last one year.

Discussion:

Cysticercosis is an infection by larval form, a common cestode, taenia solium. Man is infected by ingestion of raw and improperly cooked infected pork. Larvae have a special predilection for central nervous system. Main clinical features are headache, epilepsy, psychoneurosis, paresis or paralysis, or features of meningoencephalitis. The incubation period varies from less than a year to 30 years, average being 8 years[3]. In man cysts grow for some time and then die and tend to calcify. This happens more in muscles than in brain. Brain cysts usually measure about 1 cm[2].



CT scan of brain is an important tool for diagnosis of neurocysticercosis, and, based on location of lesions, Neurocysticercosis is classified into a) ventriculo-cisternal b) ependymal (meningeal) c) parenchymal d) mixed e) intraspinnnal, and f) cysticercus racemosus[2]. X-ray skull may show calcification (80% cases in adults and 20% in children). ELISA provides a sensitive serologic test but is not diagostic[5]. Epilepsy is an important presenting symptom of neurocysticercosis. Cysticercosis as an eitological agent for epilepsy varies from .005 to 9.6% in different parts of India[1].

Treatment of cysticercosis includes anti-cestodal drugs like praziquantel, albendazole etc[6]. For

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symptomatic patiets with neurocysticereosis both praziquantel (50 mg/kg/day in three doses for 15 days) and albendazole (15 mg/kg/day in three doses for 8 to 28 days) are effective[7]. Steroids have also been recommended in patients with brain edema, meningoencephalitis. Surgical treatment is limited to few patients presenting with mass effects and hydrocephalus[4] and during hospitalization, while on treatment ventricular obstruction may require ventriculostomy or ventriculoperitoneal shunting[7].

The patient in our study, being a muslim had no history of taking pork, but as he has been living outside the state for long duration, must have consumed pork. Neurocysticercosis is rare in Kashmir Valley but must be considered in the differential diagnosis of late onset seizures. This is more true, keeping in view the curable nature of the disease.

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PSEUDOTAMPONADE - A CASE REPORT

Parvaiz A. Zargar MD; Irshad A. Sirwal MD, DM; Bushra J.MBBS; Tajammul H. MBBS.

Abstract: A case of echo features of pericardial tamponade exaggerated by hypovolemia and reversed by volume repletion without pericardio-centesis is hereby reported.

Key words: Pericardial temponade; Pseudo tamponade; Pericardial effusion.

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Introduction

Pericardial tamponade is a potentially fatal cardiac emergency. It is because of an increase in intrapericardial pressure and is characterized by elevation of intracardiac pressure[1] progressive limitation of ventricular diastolic filling[2], and[2] reduction of stroke volume and cardiac output leading to shock[3]. When accumulation of fluid in the pericardial space causes intrapericardial pressure to rise to the level of right atrial and right ventricular diastolic pressures, the transmembrane pressure distending these chambers declines to close of zero and cardiac tamponade results. The rise of right atrial and intrapericardial pressures is less marked in the presence of hypovolemia and thus clinical features of cardiac tamponade may be masked. However, in cases of mild to moderate pericardial effusion which ordinarily would not cause cardiac tamponade, may give echo features of cardiac tamponade in the presence of hypovolemia.

Case Report

A 90 years old male was admitted to the hospital for prostatic surgery. A pre-operative echocardiography was asked by anaesthesiologist for T-wave changes on ECG and cardiac enlargement on chest radiogram which revealed normal cardiac chambers and valves with moderate pericardial effusion and severe R.V. diastolic collapse (features suggestive of tamponade).

Physical examination revealed that patient was not distressed, had decreased skin turgor, tachycardia (120 bpm), BP of 60/40mmHg without any paradox, neck veins were flat even in supine position, no hepatomegaly, and no leg edema. Cardiac examination revealed distant heart sounds, no rub or murmur; ECG revealed NSR, low voltage with diffuse T-inversion. Chest X-ray revealed cardiomegaly. Patient had rapid fluid resuscitation for few hours which resulted blood pressure to normal, with just visible neck veins in supine position that would disappear at 45° and cuff BP showed no paradox. Echocardiography was repeated after 2 days which showed similar amount of pericardial effusion without any R.V. collapse. Patient underwent uneventful prostatic surgery.

Discussion:

The triad of cardiac tamponade[1] a decline in systemic arterial pressure[2]; elevation of systemic venous pressure, and[3] a quiet heart was described by thoracic surgeon Claude S. Beck (1995).

In a series of 56 patients by Guberman et al[1] whose cardiac tamponade was diagnosed at bed side, jugular venous distension was the most common (>90%), physical finding followed by tachypnea (80%); tachycardia (77%), pulsus paradoxus (77%), total paradoxus (23%), pericardial friction rub (29%), hepatomegaly (55%), diminished heart sounds (34%) and systolic arterial pressure < 100mmHg (36%).

Echocardiography is widely used to diagnose pericardial effusion and cardiac tamponade. Echo features of tamponade include:[1] Documentation of presence and severity of pericardial effusion,[2] sudden leftward motion of septum during inspiration and an exaggerated increase in R.V. size with reciprocal decrease in L.V. size-equivalent of pulsus paradoxus,[3] diastolic R.A. and R.V. collapse or compression which may occur early during development of tamponade.[2,4] R.V. diastolic collapse appears relatively more early during hypovolemia and these echocardiographic signs of tamponade may be reversed by volume expansion[4]. The pathophysiology of these findings (also seen in this case) is that because of hypovolemia R.V. preload is very low which exaggerates the echo findings of pericardial tamponade.

Conclusion:

It follows that the recognition of patients with

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pericardial tamponade requires complementary clinical assessment to distinguish patients with various degrees of cardiac Compression from those with haemodynamic decompensation who require urgent drainage of pericardial fluid.

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PNEUMATOSIS CYSTOIDES INTESTINALIS
A CASE REPORT AND A BRIEF REVIEW OF LITERATURE

Ishtiyaq Ahmad M.S.; R.A. Laharwal M.S.; M. Ashraf M.B.B.S.; Anwar M.B.B.S.;
Nisar A. Wani M.S.; Mir Nazir Ahmad M.S., F.A.I.S.

Abstract: Pneumatosis cystoides intestinalis is a benign but relatively rare condition of uncertain etiology characterized by the accumulation of gas in the form of cysts between the layers of the intestinal wall. The cyst may be submucosal, subserosal or both. They can involve any portion of gastrointestinal tract, in particular those portions covered by serosa, as well as the peritoneal and mesenteric attachment. From there in some cases, the gas can dissect into the mesenteric veins. It has been called gas cysts of the intestine, peritoneal pneumatosis, intestinal emphysema, cystic lymphopnematosis, bullous emphasema of the intestine, interstitial abdominal emphysema, intestinal intramural gas and most often, pneumatosis cystoides intestinalis.

Key words: Pneumatosis Cystoides Intestinalis.

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Case Report:

A 46 year old male was admitted in surgery Department of S.M.H.S. Hospital in June 1999 with complaints of recurrent pain upper abdomen for last 3 years, progressive abdominal discomfort and abdominal distension for last 3 months.

Patient was on antacids and H_2 blockers for the above symptoms. For last one month patient had decreased appetite, post—prandial distension, getting relieved after induced vomiting. On examination patient had gross pallor, central abdominal distension, visible upper abdominal peristalsis from left to right and positive succussion splash. Liver dullness on percussion was obliterated. Patient was clinically diagnosed as gastric outlet obstruction. X-ray abdomen showed only gaseous distension of small gut.

Upper GI Endoscopy revealed normal mucusa with pyloric stenosis. Surgery was planned. Laparotomy was carried out and following operative findings were noted:-

1. Stomach was found hugely dilated extending low upto pelvis. (Fig I).
2. More than 70% of small bowel was replaced by multiple subserosal cysts involving whole diameter of the wall with few inches of bowel that seemed to be normal in between cystic lesions. (Fig. II).
3. There was severe stenosis of pylorus due to long standing duodenal ulcer. Patial Gastrectomy (Polya) was performed for duodenal ulcer disease. No gut resection was performed due to the extensive involvement of small gut by the disease. Moreover there was no evident intestinal obstruction. Post operative period was uneventful and patient is regularly attending the follow-up clinic without any complications so far.

Review of Literature:

Smith, BH et al[2] (1967), in their series of 35 patients with pneumatosis cystoides intestinalis, found strikingly that nearly all cases had primary submucosal involvement. Subserosal gas alone occured in only 3 cases. Pneumatosis cystoids intestinalis was always secondry to other gastrointestinal or pulmonary disease. The gas apparently passes fromthe bowel lumen through macroscopic or microscopic defects in the mucosa and muscularis muscosae. In most adults, however the condition proved to be innocuous and self limiting.

Yale CE et al[3] (1974), carried out the experiment in rats by injecting a pure culture of clostridium perfergens into either the wall of the distal part of small intestine and caecum or into the peritoneal cavity. The gas filled cysts were produced in omentum, wound, mesentery and intestine of the rats. The disorder appeared to be self limited in time, to be related to the amount of contamination,and to occur after minimal trauma to the intestines. These experiments prove that pneumatosis cystoides intestinalis can be caused by bacteria alone.

Gruenberg JC et al[5] (1977), considered pneumatosis cystoides intestinalis a disease of uncertain aetiology. Breathing high concentrations of oxygen has been promptly effective, but long-term follow—up is necessary to evaluate the continued benefit of this therapy and the minimum oxygen requirement compatible with efficaciousness and minimum risk of oxygen toxicity.

Tsiftsis DD[10] (1988), studied that pneumatosis cystoides intestinalis is a benign, relatively rare condition of uncertain etiology, characterized by the accumulation of gas in the form of cysts between the layers of the intestinal wall.

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Discussion:

The etiology of pneumatosis cystoides intestinalis has remained obscure. A mechanical therapy postulates that a primary instestinal condition such as peptic ulcer, pyloric stenosis, intestinal obstruction and scleroderma results in increased intraluminal pressure that forces gases intramurally[7].

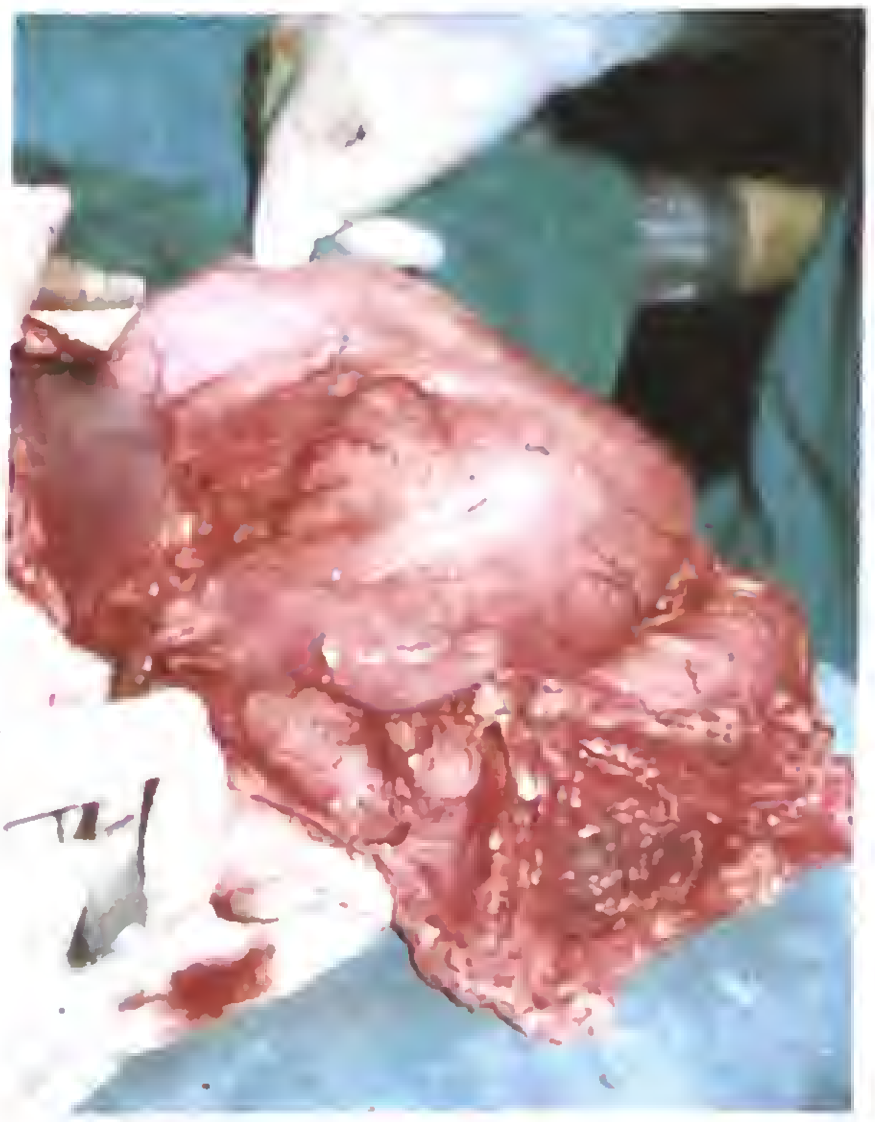

Fig. I

Another theory[4] emphasizes the association with chronic obstructive pulmonary diseases such as asthma, bullous emphysema and cystic fibrosis. According to this pulmonary theory of etiology, a painless pulmonary alveolar rupture produces a pnemomediastinum that dissects along the vessels retroperitoneally and then along mesenteric vessels to the bowel wall.

Surgical treatment[8] is indicated for the underlying primary conditions associated with pneumatosis cystoides intestinalis. Surgical treatment is also indicated for the complications of pnematosis cystoides intestinalis (obstruction, bleeding and intra-abdominal sepsis) when conservative treatment has failed. Operation is directed to the etiological cause of complication, and is not influenced by the extent of pneumatosis. Removal of worse affected segment of intestine usually results in remission of the remaining lesion.

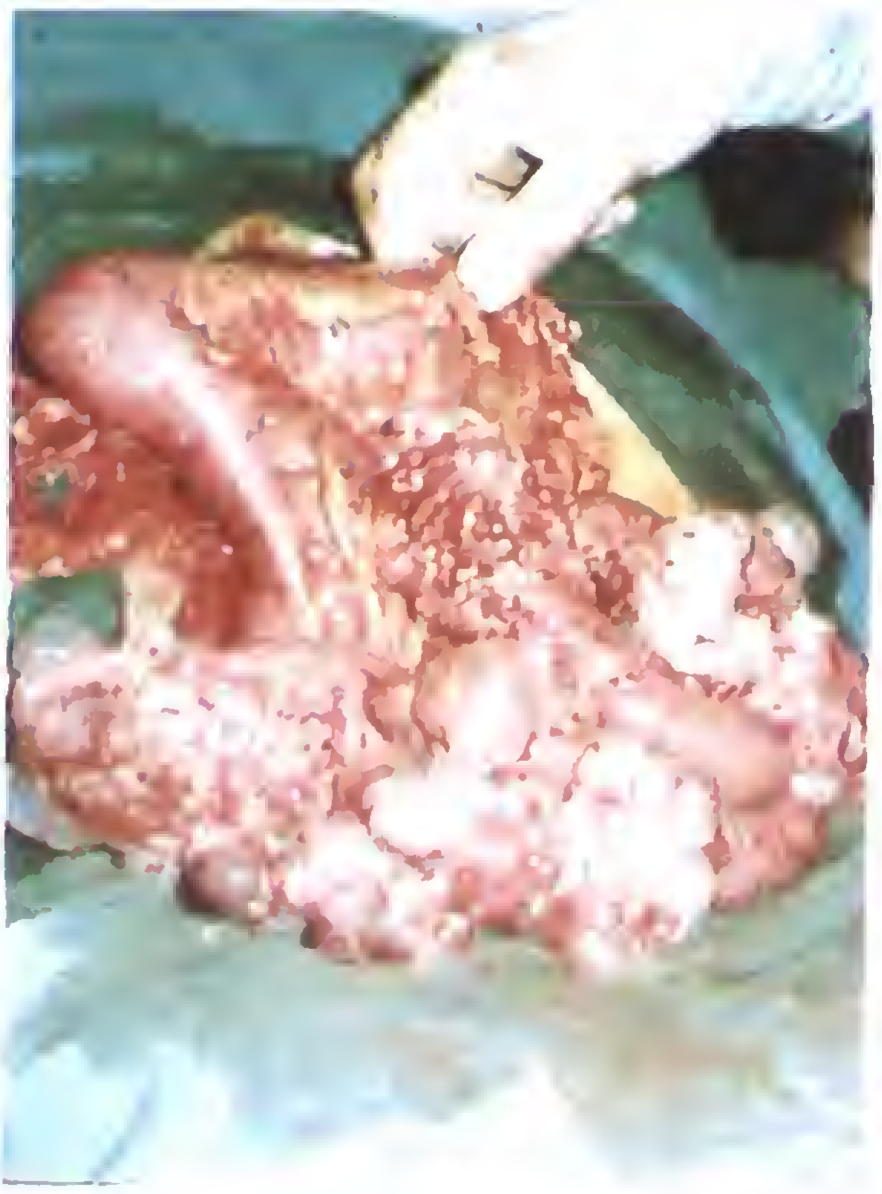

Fig. II

Metronidazole[10] has been used with success given a pulsed doses for 5 days every 2-3 weeks. The successful use of this drug as an antimicrobial agent suppressing aneroabic bacteria may support the thesis that gas forming bacteria contribute to pneumatosis.

The use of oxygen[10] to treat pneumatosis cystoides intestinalis is based on the theory that partial pressure of gases within the cyst must be in a equilibrium with that of the same gases in the blood capillaries, though the intracystic pressure might be somewhat greater than the atmospheric pressure. Cystic gas contains mainly nitrogen, with lesser concentration of Carbon dioxide, Hydrogen and Oxygen. Breathing oxygen in high concentration decreases the partial pressure of nitrogen and Carbon dioxide in the capillary blood, creating a pressure gradiant between the cyst and capillary blood gases. This results in the diffusion of nitrogen, Hydrogen, Carbon dioxide from the cysts into the blood and emptying of the cysts.

However oxygen therapy must be applied with caution since pneumatosis cystoides intestinalis is associated with pulmonary disorders. In patients with Chronic hypoxic lung disease, hyperoxygenation has the risk of Carbon dioxide intoxication. Oxygen treatment should also be avoided in patients with serious intra-ocular problems in neonates.

In our case the underlying cause of pneumatosis cystiodes intestinalis was long standing duodenal ulcer complicated by pyloric stenosis.

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PERFORATION OF INTRA UTERINE DEVICE (IUD)

M. Saleem Wani M.S.; K. Alam Wani M.S.

Abstract: Intra terine device (IUD) is highly effective and safe form of coontraception, but obviously is not without adverse effects and complications. We present two cases of perforation of IUD.

Key words: Intra uterine device, Uterine perforation.

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Introduction:

Intrauterine devices are safe and effective method of contraception. According to history of contraception, the first intrauterine devices (IUD's) were inserted into female camels. Turks and Arabs learned that inserting pebbles through hollowtubes into uteri of their female camel would prevent them from conceiving during long trips across the deserts[1]. The first reference to use in human female came from Hippocrates who wrote about the contraceptive possibilities of placing foreign bodies into the uterus. The first documented use by women apparently occured in eleventh century as recorded by Avicenna - an Islamic Scientist. Over the past decades, mounting evidence has confirmed the extremely high contraceptive effectiveness of IUD's as well as some of the risks associated with their use. We report two cases of Uterine perforation with translocation of IUD into peritoneal cavity.

Case Report No. 1:

A 30 years, multiparous female presented with recurrent lower abdominal pain of nine months duration. The patient had history of insertion of copper IUD elevent months back. At the time of insertion of IUD the patient had noticed moderate pain and bleeding p/v for two days. Thereafter, the patient was doing well except for mild degree of recurrent pain in the lower abdomen, at times colicky in nature, which would resolve with antispasdmodics. Gynaecological examination after one month of insertion of IUD revealed presence of IUD in-situ. Thereafter patient never reported to the Gynaecologist for follow-up. When she was examined nine months latter for severe pain in the lower abdomen p/v examination revealed absence of Tails of IUD. X-Ray Abdomen revealed IUD lying outside the uterine cavity opposite L4-L5 in the mid line (Figure I).

At Exploratory laprotomy the IUD was found embedded in dense adhesions in the anterior abdominal wall around the umbilicus. Rest of the laprotomy was normal. The IUD was removed after lysis of adhesions. The patient made an uneventful recovery.

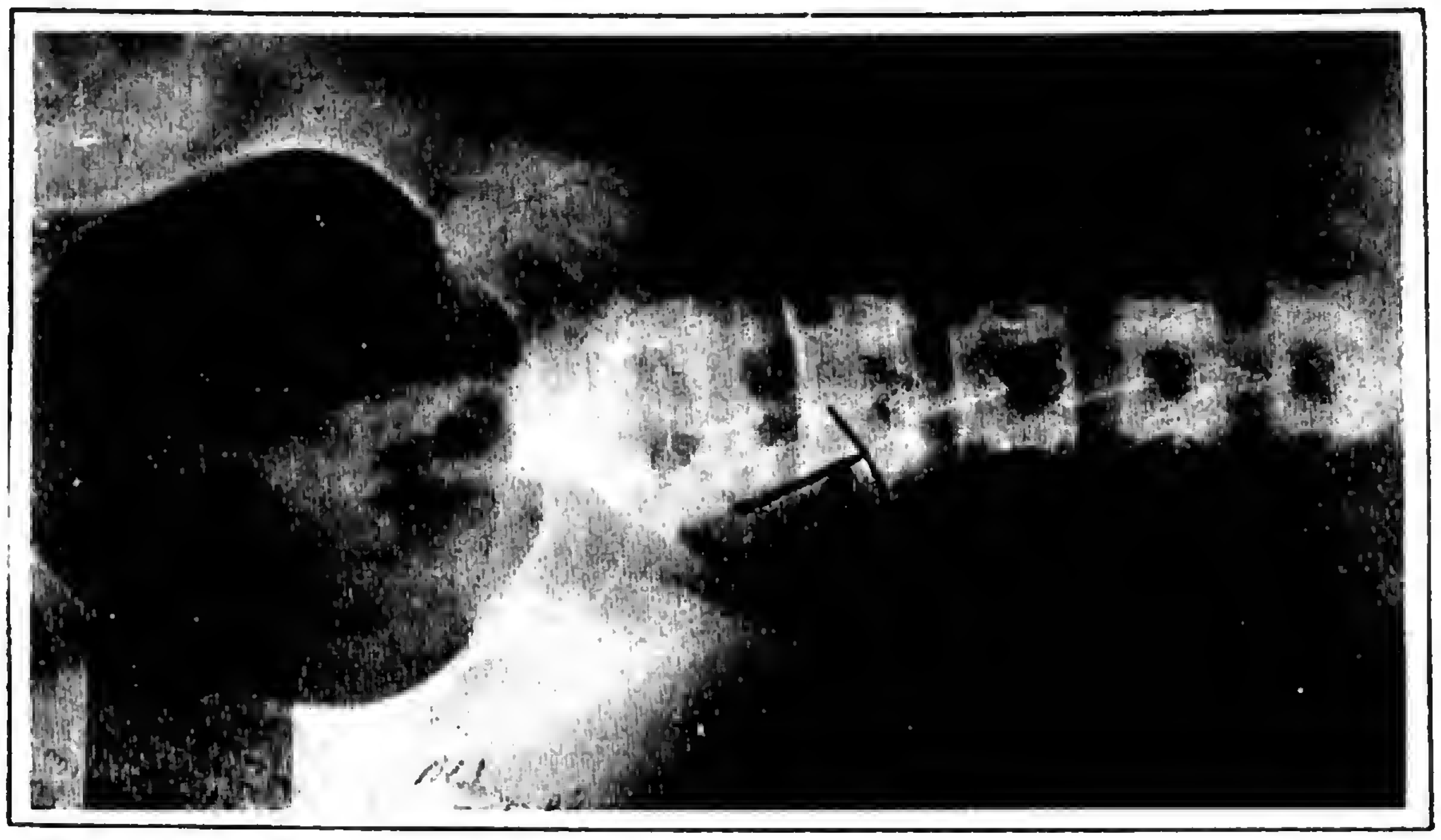

Fig. I

Case Report No.2:

A 28 year old, para two female presented with pain lower abdomen and dysuria one week after insertion of copper - IUD. Pervaginal examination revealed absence of tails of IUD in the Vagina. At ultra sound examination of the abdomen, the IUD was found lying outside the uterine cavity near the dome of urinary bladder.

AT laprotomy, one limb of IUD was found partially perforating the urinary bladder wall with Omentum sealing it from the peritoneal cavity. The IUD was removed and rent in the bladder wall closed in layers. Post operative period was uneventiful.

Discussion:

The IUD is highly effective form of contraception. IUD's have been popular method oof birth control[2,3].

However, IUD is not without adverse effect and

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complications. The overall morbidity and mortality rates remain low with intrauterine contraception; hospitalization ranging from 0.3 to 1.0 per 100 women years of use, and deaths range from 1-10 per millioon women years of use[4].

The various adverse effects and complications encountered with IUD's are problems associated with insertion, in the form of pain, discomfort, spontaneous expulsion of IUD, cramping, bleeding and pelvic inflammatory diseases. One of the major side effects of intra uterine contraception is perforation through uterine wall into the pelvic or abdominal cavity properly described as translocation of the device. The incidence of this complication ranges from 0.1 - 8.7per one thousand insertions and is directly proportional to the skill of individual performing the insertion[1,5].One major reason for perforation is failure to establish the size and orientation of the uterus by careful pelvic examination[5].

The complications occur most frequently at the time of insertion, hoowever, perforation is most often silent and is not recognised untill somewhat later when it is found that the tail has disappeared or when a pregnancy is diagnosed[4]. In this instance the perforation usually begins at the time of insertion and the device is subsequently forced by the uterine contractions through the remiander of the uterine wall into the peritoneal cavity[5,6]. Perforation of IUD into the urinary bladder with stone formation around the IUD has been reported.

Copper IUD's must be taken out as soon as possible because copper ions induce intense reaction resulting in dense adhesions and intestinal obstruction[7]. Laproscopic removal of the device can also be done[5,6]. IUD from within urinary bladder can be removed cystoscopically.

Intrauterine device is the highly effective and safe formof contraception but obviously is not without adverse effects and complications. The risk of perforation can be avoided by careful insertion of the device and avoiding the insertion in the earlypost partum period[1,9]

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ASPIRIN USE AND REYE'S SYDROME: A CASE REPORT

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Abstract: Reye's syndrome is an acute metabolic ecophalopathy of unknown etiology associated with visceral - mostly hepatic dysfunction that is not attributed to any infection, inflammatory disorder or inherited metabolic defect.

It is seen primarily in children though infant and adult cases have been reported. The encephalopathy has been associated with antecedent viral infection especially varicella and influenza A &B. Clusters of cases have been associated with influenza B outbreaks. There is also an association between this encephalopaty and aspirin use in children. The decfine in the incidence of this disease may be because of this awareness and the avoidance of aspirin in children suspected to suffer from these viral prodromes.

Here we report the case of a child who developed features of the syndrome after theapeutic use of aspirin for rheumatic fever.

Key words: Reye's Syndrome, Micro vesicular steatosis, Intracraial pressure.

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Case Report:

6 year old boy presented to the paediatric outdoor with Complaints of fever and arthirtis of 5 days duration, The arthirtis was typically migratory involving first ankes and then knees. There wasno rash; dyspnea, palpitation; cough; sore throat; abdominal pain, or dysuria.

Physical examinatin revealed an ill child with arthritis of both knees. Both the joints were swollen and tender with muffled heart sounds. Rest of the examination was normal.

ASO titer was raised, CRP was positive and ESR was 32mm in Ist hr. The chest X-ray and ECG showed no abnormality.

A presumptive diagnosis of rheumatic arthritis with mild carditis was made and the child was put on Aspirin. The child improved in three days and was discharged on the same treatment.

After continuing treatment for 2 weeks, the child presented with repeated vomiting and drowsiness.

When examined, the child was in grII coma, mildly dehydrated and had dilated pupils. The cardiac murmur was still present. There was no organomegaly, no evidence of meningeal irritation and no neurodeficit. Fundus examination showed Papilloedema.

Biochemical Investigations were as under:

Hb.	11.6 gm/l	Prothrombin time	19 seconds (control-12 sec.)
Counts	$2.6x10^9/mm^3$		
PLT	$350x10^9/mm^3$	PTI	63.1%
DLC	P61 L 39	Serum bill.	0.87%mg%
PBF	Normocytic, Normochromic.	Alb	3.7gm%
		SGPT	329 units (N 0 - 40 units)
ABG		ALP	319 units
- PH 7.312		Blood Sugar	30.7 mg%
PC02-35.6		CSF Examination:	within normal limits.
P02-86.1			
HC03-17.6			
SAT-93%			

On the basis of clinical manifestations and biochemical data, a diagnosis of Reye's syndrome with rheumatic carditis was made and child managed with IV dextrose, mannitol and steroids. A repeat blood sugar on second day was normal and the child had uneventful recovery within 4 days. However, steroids were continued in view of rheumatic carditis.

Discussion:

Reye's Syndrome is a metabolic encephalopathy that has been associated with viral infection and aspirin use[1,3].

The disease has a biphasic course. As he seems to be recovering froom the viral illness, there is repeated vomiting and the child becomes lethargic and irritable. This is stage I of the disease[2,7].

In stage II there is further neurologic deterioration with hyper reflexia, seizeres, come, autonomic disturbances[2,7].

In stage III there is decorticate posturing and stage IV is marked by decerebrate posturing and deep coma while in stage V, the brain stem reflexes are lost and

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death may follow or the patient may recover at any stage of the disease[2,7].

Hepatic dysfunction is common but jaundice is rarely seen. Hepatotoxicity other than Reye's syndrome is well documented with aspirin use[9].

Hypoglycemia is seen in about 1/3rd of children. Coagulopathy is unusual but needs to be monitored[5,7].

Serum ammonia is elevated. CSF examination is normal but elevated intracranial pressure is seen in patients beyond stage II[2,7].

Liver biopsy reveals diffuse hepatic microvesicular steatosis and lack of necrosis or inflammatory infiltrate[1,5]

Treatment is similar to that of acute hepatic failure i.e., supportive. The mainstays of treatment are control of increased ICP, careful hydration, prevention of hypoglycemia and correction of electrolyte disorders.

The disease should be kept in mind in any child with febrile illness and aspirin use and aspirin as an antipyretic preferably avoided.

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STATUS REPORT: CANCER ESOPHAGUS IN KASHMIR

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Cancer is a frightening name that can unnerve any person, but it remains a common ailment that can strike both young and old. Over the years, major advances have been made in understanding the cause and treatment of many cancers. In fact, a number of cancers of the body are curable particularly if detected at an early stage of disease. Of significance in this group are cancers involving blood cells (leukemia) and lymph nodes (lymphoma). However, a number of cancers in the body have no known cause and have no suitable treatment.

Another important aspect of many cancers is their varied prevalence from one region of world to another. In the United States, cancer of lung is the most common in males and cancer of breast in females. In Africa and many countries in Southeast Asia, cancer of the liver is a major killer disease. Japan is known for having high incidence of cancer stomach. Cancer of esophagus is an uncommon cancer in the western Europe and North America, with an incidence (new cases with disease) of less than 6 per 100,000 population per year in men and 1.6 per 100,000 population per year in women. However, this cancer is common in China and many other countries around the Caspian Sea. The reason for this high incidence of cancer of esophagus in these regions of the world is not known. Extensive studies by many international organizations have failed to incriminate a single causal agent for high incidence of cancer esophagus in such countries.

Cancer esophagus is a devastating disease and strikes people in their middle or late middle age. The disease presents as difficulty in swallowing (dysphagia) solid food like rice and bread. Dysphagia to solids is of short duration and over a period of few weeks to months person cannot even eat or drink liquids and develop starvation and dehydration, unless an effective treatment is instituted (table 1). Unfortunately by the time difficulty in swallowing ensues, the disease has gone into advanced stage and only palliative measures can be done to relieve symptoms temporarily. Cure at this stage of disease is uncommon.

The physicians practicing in Kashmir in the past have in their day to day practice appreciated common occurrence of cancer esophagus in this region. Patients with cancer esophagus constitute a substantial percent of consultations to the general physician, ENT specialists and gastroenterologists. To draw a point in this direction one may refer to surgical biopsies seen at Sheri-Kashmir Institute of Medical Sciences Soura Srinagar Kashmir over a period of 3 years (December 1982 to December 1985). Of the 8060 surgical biopsy specimens evaluated in this period, 2340 (29.0%) were diagnosed as having cancer of various organs. 68.7% of these cancers had occurred in the gastrointestinal tract namely- esophagus, stomach, colon, pancreas and gall bladder. Around 46.1% of the gastrointestinal cancers were situated in the esophagus (1). These exceptionally high figures of cancer esophagus in the surgical biopsy specimens speak volumes of the load of this disease in Kashmir. However these data were of crude nature and could not be presented to the rest of the world and International organizations to draw attention for further studies in this area.

Table-1. Signs and Symptoms of Advanced Cancer Esophagus

Symptom	Significance
Dysphagia	Lesion obstructing lumen
Pain radiating to the back on swallowing	Extra-esophageal infiltration
Dysphonia	Laryngeal paralysis
Diaphragmatic paralysis	Involvement of phrenic nerve
Coughing when swallowing	Tracheo-esophageal fistula
Superior Venacaval syndrome	Spread to mediastinum
Palpable supraclavicular or cervical lymphnodes	Metastatic spread
Malignant pleural effusion Malignant ascites.	Metastatic spread
Bone pain.	Metastatic spread

To study the load of cancer in a community we need incidence (new cases per 100,000 per year) of the disease by collecting data in a more scientific manner. From 1983 onwards, Department of Gastroenterology at the Sheri-Kashmir Institute of Medical Sciences, Srinagar was involved in a number of systematic studies to find incidence of cancer esophagus and its possible causes. We also attempted to define the mechanism by which

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various factors could lead to the evolution of this disease.

We performed a study on incidence of cancer esophagus in the valley[2]. The entire population of Kashmir was studied and all new cases of esophageal cancer were recorded. 1515 cases of esophageal cancer had occurred over a 3 year period from July 1986 to June 1989. Of these 1050 cases were men and 465 cases were women. The disease occurred in the age group of 45-70 years. Crude incidence rate of the disease was 22.6 per 100,000 per year in men and 11.5 per 100,000 per year in women. Age specific incidence rate is shown in Fig 1 and peaked to 198 per 100,000 per year in men of 60 - 64 year age group and 248 per 100,000 per year in women of 70 to 74 age group. Truncated incidence rate (35 to 64 year age group) was 108.2 per 100,000 per year in men and 70 per 100,000 per year in women. Age standardized incidence for the disease was 44 per 100 000 per year in men and 30 per 100 000 per year in women. These figures were 3 to 6 times higher than those recorded by cancer registries in Banglore, Madras and Bombay (Fig 2): These high incidence figures were comparable to incidence of esophageal cancer occurring in the northern regions of Iran, Turkmenia, Kazakhstan, Uzbekistan and China (Table 2). An esophageal Asian cancer belt has been defined extending from northern Iran, Mongolia, Central Asia and Japan. Our study showed that Kashmir borders this cancer belt on the southern region. At the same time Kashmir also had an unprecedented high incidence of gastric cancer.

Table 2 .Age Standardized Incidence Rates for Esophageal Cancer from Iran, USSR and Kashmir

	Esophageal Cancer		
	Men	Women	M:W
Iran			
Gonabad	93.1	110.0	0.8:1
Gorgan	66.6	49.2	1.3:1
Gilan	20.1	6.2	3.2:1
USSR			
Turkemenia	51.1	33.2	1.5:1
Kazakhstan	47.8	26.3	1.8:1
Uzebekistan	28.5	13.7	2.0:1
Kashmir			
Islamabad	70.0	25.0	2.8:1
Srinagar	54.5	26.2	2.0:1
Kupwara	17.0	16.0	1.0:1

One of the hallmarks of this study was varied incidence of esophageal cancer in different districts and various ethnic groups in Kashmir. The incidence rates for esophageal cancer in Southern district of Kashmir, Islamabad were 4.1 to 5.4 times higher in men and 1.5 to 2.0 times higher in women than those for Northern district, Kupwara (Fig 3). The incidence rates for esophageal cancer in Muslims, Hindus, and Sikhs were different (Fig 4).

These figures for the first time established Kashmir as a high incidence zone of esophageal cancer. Considering this high incidence of esophageal cancer in Kashmir, another study was done to define the evolution of this disease and this study showed that esophagus of people of Kashmir is abnormal in most of the adult population[3]. This study was done in otherwise healthy volunteers who opted to undergo assessment of their food pipe for promotion of scientific knowledge. Of the 107 volunteers studied, a chronic form of esophagitis (inflammation of esophagus) was seen in 2/3rd of subjects. These subjects had no symptoms related to their esophagus. Around 1/3rd of the subjects had more advanced changes in their esophagus namely mucosal acanthosis, atrophy and dysplasia. Dysplasia is a pathological state that occurs in tissues before a cancer is formed. Many tissues in the body pass through various grades of dysplasia eventually leading to a cancer. Around 10% of the volunteers studied had changes of dysplasia in their esophagus. These data have been of value in understanding pathogenesis of cancer of esophagus in Kashmir. We believe that a chronic form of esophagitis exists in majority of the population in Kashmir. The esophagitis leads to dysplasia and eventually culminates into cancer. This process can take up-to 20 to 30 years. Over these years persons have no symptoms related to this form of esophagitis and dysplasia. Even the early cancer once developed cause no symptoms. The symptoms only occur when the cancer blocks the lumen of the esophagus and does not allow swallowed food to pass into the stomach. At this stage the disease is advanced and only amenable to palliative treatment and not cures (Fig 5).

Kashmir is an ethnically distinct population with special personal and dietary habits (table 3). These include intake of sun dried cruciferous vegetables of brassica family (Hakh), pickled vegetables (Aanchar), dried or smoked fish (Hokh / fur-gard), cakes made of chilies, garlic and cardamom (Wur) and above all large quantity of hot salt tea (Noon chai). Smoking in the Valley is also distinctive and involves use of a hubble-bubble (Jajeer). Could any of these habits of the people lead to high incidence of esophageal cancer in the Valley? Although speculated, till recently there were no scientific data to prove the point that one or more of the above personal or dietary factors could be implicated for high incidence of esophageal cancer in the Valley.

Recently, we have performed case control study in patients with esophageal cancer to define if there are any personal or dietary factors which can explain high incidence of esophageal cancer in the valley (4). For this we had a detailed assessment of 100 patients with proven

Table 3: Special Personal and Dietary Habits of Kashmiri Population

Habit	Characteristic	Significance
Hot salted tea (Noon Chai)	green tea leaves are brewed in sodium bicarbonate until a thick red brown colored extract is obtained. extract is diluted with water and salt and milk added. tea is repeatedly boiled in a Samavar and drunk while boiling hot.	hot tea may cause thermal burn, contains N-nitroso compounds (known carcinogens)
Green tea (Kehwa)	prepared by boiling green tea in Cardamom. Cinnamon and Saffron	may cause thermal burn
Sun dried vegetables (Hakh)	vegetables are sun dried in summer, stored and used in winter months	high nitrate content, may cause endogenous nitrosation and formation of nitrosamines, known carcinogens
Red chilli cakes (Wur)	cakes made of chilli, garlic and cardimom and used in large amounts for food preperations	direct mucosal injury, high content of amines, endogenous nitrosation may form nitrosamines known carcinogens
Pickled vegetables (Anchar)	vegetables,chilli and other condiments mixed with vinegar and allowed to ferment for weeks and use in large quantities	direct mucosal injury, high content of amines, endogenous nitrosation may form nitrosamines known carcinogens
Hubble-Bubble (Jajeer)	tabacco smoked through a pipe, smoke passes through water filled container,	known association with cancer esophagus
Dried /smoked fish (Hokh/fur-gard)	sun dried or smoked fish is used	high amine/nitrate content, endogenous formation of nitrosamines, known. carcinogen.

esophageal cancer and compared it with 200 age and sex matched controls. The controls were relatives of such patients or healthy persons from the same localities. Patients with esophageal cancer when compared to controls had less consumption of fresh fruits and vegetables and increased intake of pickled vegetables (Aanchar), chilly cakes (Wur), smoked fish and sun dried leafy vegetables. In addition patients with cancer when compared to controls had consumed larger quantities of salt tea (Noon chai). Also patients with cancer were more often smokers and had smoked larger amounts of tabacco through hubble-bubble (Jajeer). To reduce the impact of confounding factors we performed a multivariate analysis and based on this the factors which had association with esophageal cancer were: 1) intake of more than 5 cups of salt tea per day, 2) smoking, 3) less intake of fresh fruits (<6 times per month). Patients who consume salt tea more than 5 cups /day had an odds ratio of 6 for the development of the disease (Table 4). It was the amount of tea, which was important rather than the temperature at which it was drunk.

While analyzing the above data we must caution that nature of study (case control study) does not conclusively prove cause and effect relationship of these dietary and personal habits to esophageal cancer in the Valley. To prove cause and effect relationship of one or more of the implicated factors we had planned longitudinal and intervention studies but were abandoned for reasons beyond our control.

Table 4: Multivariate Analysis of the Factors Attributing to Cancer Esophagus

S. No.	Factor	Odd's Ratio	Attributable Risk (%)
01	More consumption of tea (> 5 cups/day)	5.93 (0.59-0.79)	59.42
02	Smoking (cigarettes, Hukka)	4.74 (0.50-0.70)	60.00
03	Less consumption of milk (< 300 gms/day)	1.92 (0.41-0.57)	32.65
04	Less consumption of fats and oils (< 30 gms/day)	1.92 (0.39-0.59)	32.65
05	Less use of fruits (< 6 times per month)	2.40 (0.30-0.54)	46.51
06	All (1 to 5)	13.50 (0.59-1.05)	69.51

However these data at best could be an eye-opener and demanded further inquiry as to why salt tea should lead to such a high incidence of esophageal cancer. With the help of a number of international agencies analysis of the various food items special to Kashmir were analyzed.

Analytical data on aliphatic amines and nitrates from the most commonly used fresh and sun-dried vegetables, red chilies and a widely consumed beverages, and salted tea consumed by the inhabitants of Kashmir were done and reported (5) Exposure estimates for the adult population showed that high consumption of boiled Brassica vegetable leads to a high nitrate intake of 237 mg/day. The frequent consumption of hot salted tea resulted in exceptionally high exposure to methylamine (1200 micrograms/day), ethylamine (14,320 micrograms/day), dimethylamine (150 micrograms/day) and diethylamine (400 micrograms/day). The indiscriminate use of red chilies in the area leads to exposure to dimethylamine (280 micrograms/day), pyrrolidine (517 micrograms/day) and methylbenzylamine (40 micrograms/day). This was the first report where a chronic exposure to methylbenzylamine has been shown in a population at high risk of esophageal cancer.

Fig 5: Evolution of mucosal changes from normal esophagus to cancer

Mucosal Changes	Symptoms
Normal Mucosa	No
Esophagitis	No
Dysplasia	No
Carcinoma in situ	No
Early cancer esophagus	No
Advanced cancer	Dysphagia (rapid progression)

Salted tea prepared by adding sodium bicarbonate showed high methylating activity (equivalent to 3-PPM N-methylnitrosourea) upon in vitro nitrosation. Pure caffeine treated under conditions of the tea preparation formed caffeidine and caffeidine acid. The formation of two new compounds mono-nitrosocaffeidine, an asymmetric nitrosamine, and dinitrosocaffeidine, a N-nitrosamide was reported on in vitro nitrosation of caffeidine. Mononitrosocaffeidine was also found after nitrosation of the typical Kashmir tea. The nitrosation of caffeidine acid produced N,N'-dimethyl-parabanic acid, mononitrosocaffeidine and N-N'-dimethyl-N-nitrosourea. In view of the well-known structure-activity relationships of these N-nitroso compounds, their possible endogenous formation due to high consumption of salted tea may be a critical risk factor for the high occurrence of esophageal and gastric cancers in Kashmir[6].

Although the story of esophageal cancer in the Valley has unfolded, yet it will take years of painstaking hard work to collect epidemiological data to implicate any one or more of the food and personal habits in its causation. Also we need more basic work in the laboratories to screen a wide range of food items for possible carcinogens. When any of the items is confirmed to cause this cancer mass educational program to public is needed to reduce the incidence of this devastating disease in this community. Till that time it is safe to propose following advice to the inhabitants of the Valley:

1. Limit intake of salt tea to less than 5 cups per day,
2. Stop any form of smoking
3. Take fresh fruits at least once in a week.

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MULTICENTRE CLINICAL EVALUALTION OF "EAZMOV PLUS" A POLYHERBAL FORMULATION IN ARTHRITIC PATIENTS

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Abstract: *A multicentre Clinical Observation and Monitoring Project (COMP) was carried out in 60 patients of Arthritis comprising Osteo arthritis (OA), Rheumatoid arthritis (RA) and Non-specific Arthritis (NSA), ranging in age from 32 to 70 years. This trial was designed as a prospective observational study to monitor the safety and efficacy profile of "EazMov Plus" a polyherbal formulation for treatment of Arthritis. It involved 10 physicians from different parts of Northern India who recruited arthritic patients and no maximum limit of patients per physician. Thus this COMP ensured the use of the product in "Real Life Situation", as seen in day to day clinical practice. The Clinical profile of all patients was carefully recorded in a clinical examination form at the beginning of treatment and "EazMov Plus" Capsules were given in dose of 1 Capsule twice a day after meals for 3 weeks. Clinical signs were again recorded at the end of week 1, 2 and 3 respectively on a scale as absent, mild, moderate and severe. Patient compliance, the presence of side effects, and overall response to treatment were carefully observed and noted. Significant reduction in the severity of symptoms as compared to the baseline was seen, with improvement in joint mobility and reduction of stiffness. The incidence of drug related adverse events was minimal <3% and did not require discontinuation of treatment. It would be interesting to compare the resultsof this real life COMP with a double blind activedrug/placebo controlled trial in a monitored clinical environment.*

Key words: *Eazmov; Herb; Arthritis*

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Introduction

Osteoarthritis (OA) is the most common joint disease of humans. Erroneously called degenerative joint disease it represents failure of a diarthrodial (Moveable, synovial lined) joint. In idiopathic (Primary) OA, the most common form of the disease,no predisposing factor is apparent. Secondary OA is pathologically indistinguishable from idiopathic OA but is attributable to an underlying cause[1]

Risk factor for OA (Adapted after Hochberg, 1984)[2,3]

a) Age
b) Female Sex
c) Race
d) Genetic factors
e) Major joint trauma*
f) Repetitive stress, eg, vocational*
g) Obesity*
h Congenital / developmental defects*
) Prior inflammatory joint disease
j) Metabolic/endorcine disorders.

**Potentially modifiable*

Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown cause. Although there are a variety of systemic manifestations, the characteristic feature of RA is persistent inflammatory synovitis usually involving peripheral joints in a symmetric distribution. The potential of the synovial inflammation to cause cartilage destruction and bone erosion and subsequent changes in joint integrity is the hallmark of the disease (Lipsky, 1998)[4].

The goals of therapy in arthritis treatment are i) Relief of pain ii). Reduction of inflammation iii). Protection of articular structures iv)Maintenance of function andv) Control of systemic involvement. Also of prime concern to the treating physician is the control of the degenerative process affecting the articular and para-articular structures which can continue unabated despite NSAID usage and even pain relief.

Conventional therapy today is palliative with Non-Steroidal Anti-inflammatory drugs (NSAIDs) forming the mainstay of treatment. However, concern is growing with respect to the appropriateness of NSAIDs administration because of the side effects especially thos erelated to the gastrointestinal tract, renal and hepatic functions. The segment of the society with highest incidence of arthritis i.e. the elderly population appears to be at greater risk for gastrointestinal and other side effects and the annual rate of hospitalisation for Peptic Ulcer disease among NSAID users was 16 per thousand, 4 times greater than that for subjects not taking NSAIDs. Upto 30% of all hospitalizations and deaths related to

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Peptic Ulcer disease have been attributed to NSAIDs use[5].

Thus inspite of giant strides in the development of management modalities for arthritis the inadequacies and limitations of NSAIDs are often exposed and no causal therapy exists. Frustration with conventional chemical medicine is driving the people towards satisfying plant based medicines[6,7]. This trend prompted the formulation of "EazMov Plus" by Envin Bioceuticals Pvt. Ltd. Sharanpur containing the standardized extract of Picrorhiza kurroa, Tinospora cordifolia, Glycyrrhiza glabra, Zingiberofficinale, Cyperus rotundus, Saussurea lappa and Boswellia serrata, in their optimum concentrations[8].

Preclinical and Clinical evaluation has established the safety and efficacy of this formulation in the treatment of rheumatic disorders in controlled laboratory and clinical conditions[9,10,11].

Despite the widespread use of herbal medicines by the Indian population, published Indian Data in this area is scarce, hence it was decided to conduct a Clinical Observation and Monitoring Project (COMP) on "EazMov Plus" in patients of Arthritis comprising Osteo arthritis (OA), Rheumatoid arthritis (RA) and Non specific arthritis (NSA).

Patients and Methods

The study was designed as a prospective observational study to monitor the safety and efficacy profile of "EazMov Plus". The primary requirement for patient inclusion was suspected clinical picture of arthritis under actual field conditions encountered by the medical practitioner in a busy outdoor general practice.

No maximum limit of patients was fixed per physician. Thus the design of COMP ensured the use of EazMov Plus in "Real Life Situation as seen in day to day clinical practice. This study involved 60 patients and 10 physicians from different parts of Northern India.

Clinical Sings:

The clinical profile of all patients at the beginning of treatment (Taken as day Zero) was carefully recorded by the physicians in a clinical examination from Age, Sex, and clincial history of the patients, with clinical signs and symptoms and diagnosis were recorded. These were graded on an arbitrary scale of pain severity, morning stiffness, joint swelling, disability and/or loss of function due to joint deformity (Table-I). Gradation of symptoms was recorded as absent, mild, moderate and severe on day Zero, and at the end of week 1 and at the end of study (Week 3). Patient compliance with regard to the presence of side effects and overall response to treatment were carefully observed and recorded at the end of week 1,2 and 3 of treatment.

Table-I: Scoring of Signs/Symptoms Severity - (ARA Criteria)

Score/Grade	Pain Intensity	Morning Stiffness	Functional Limitations
0	Pain absent	Less than 25 mts	Not present
1	Mild	15-30 minutes	Mild limitation
2	Moderate	31-60 minutes	Moderate swelling
3	Severe	> 60 minutes	Gross swelling

Laboratory Investigations

Blood was collected from patients who participated in the study immediately after clinical examination i.e. on day Zero and examined for Rheumatoid Factor (RF), Serum Uric acid (UA), Erythrocyte Sedimentation Rate (ESR Wintergreen's method), and other specific tests as required by patient's clinical condition (viz. Blood sugar). RF, UA and ESR were again repeated at the end of the 3 week's trial period. Radiological examination by way of x-ray films of the affected part was done where required to establish the diagnosis.

Adverse Events and Adverse Effects

Adverse events were defined as any occurence of a medical nature that was reported by the patient or discovered by the doctor while the patient was receiving "EazMov Plus" and they were duly recorded. Similarly any adverse effects of the drug were also recorded.

Treatment

All patients were given 1 Capsule of 550 mg of "EazMov Plus" twice a day (morning and evening) after meals for 3 weeks. No concurrent medication was given to any patient for either joint pain or stiffness, however any associated medical condition was managed as per standard guidelines viz, Diabetes mellitus was treated with oral hypoglycaemic agents and hypertension with antihypertensive drugs which the patient had been routinely taking.

Patients with evidence of impaired renal function, hepatic or cardiac dysfunction, pregnancy or nursing mothers were excluded from the study. Women in the reproductive age group were advised to practice barrier contraception. Patients were informed about the trial medication being used and informed written consent was obtained for willingness to try this herbal medication.

Mean Severity Scores

The clinical signs and symptoms assessed were i) Pain severity ii) Morning stiffness iii) Joint swelling and vi) Loss of function. Response to treatment was evaluated by the improvement in these signs and symptoms by the end of week 1 and week 3 of treatment. Each sign/ symptom was scored as absent (0), mild (1), moderate^{2} and severe^{3}. The mean severity scores were calculated and significance was compared with the baseline at 5% confidence limit, using Student's 't' test.

Biochemical and Haematologlical Changes

ESR was noted at the end of Ist, 2nd and 3rd week after commencing treatment.

Global Assessment

Global assessment of all patients was done on a four point scale as excellent, good, fair and poor at the end of the 3rd week of treatment.

Results:

Of the 68 patients enrolled 18 were males and 50 were females. Table-2 gives the demographic data. There were 8 drop outs who did not complete the study due to various reasons. 60 patients, 32 to 70 years of age, were analysed, and out of these 46 were female and 14 were male. Clinical examinatioin and laboratory and radiological examinations showed that there were 32 cases of Rheumatoid arthritis (RA), 16 of Osteo arthritis (OA) and 12 falling into the category of non-specific arthritis (NSA) which included conditions such as Ankylosing Spondylitis, Reactive arthritis, Psoriatic arthritis, Gout and others (Table 3).

Table-2: Demographic Data

Patients enrolled	68
Drop outs	8
Patients under trial	60
Male	14 (23.3%)
Female	46 (76.6%)
Age Range (Yrs)	32-70 yrs.

Table-3: Disease Distribution in Patients under trial

Arthritis patients	60
Rheumatoid Arthritis (RA)	32 (50.3%)
Osteo Arthritis (OA)	16 (26.6%)
Non-Speicfic Arthritis (NSA)	12 (20%)

60 (100%) of the patients had joint pain, while 52 (86.6%) had morning stiffness and joint swelling and 48 patients (80%) showed limitations of function due to joint deformity and pain at the beginning of the study (Table 4).

As seen in Figure 1, the percentage reduction in the signs and symptoms was 34.6% for joint pains during the first week, 52% during the 2nd week and 75.3% during the 3rd week. For morning stiffness and swelling the relief percentage during the treatment period was 28% during the first week, 49% during the second week and 78.7% at the end of the treatment. 26.2% of the patients showed improvement in function during the first week and this increased to 46.49% at the end of 2nd week and 68% at the end of the study, respectively. Mean severity scores for joint pains and morning stiffness showed relief at the beginning of week 1 'P' value < 0.05 and highly significant relief ('P' value >0.001) at the end of 3 weeks. However, functional disability was relieved in a majority of cases only at the end of 3 weeks (Table 5).

Table-4: Clinical Profile of Patients on Admission

Signs / Symptoms	No. of Patients
Joint Pain	60 (100%)
Morning Stiffness & joint Swelling	52 (86.6%)
Limitation of Functions	48 (80%)

Table-5: Mean Severity Scores of Signs/Symptoms During Treatment

Signs/Symptoms	Mean Severity scores ± Standard error		
	Day -	At the end of Week 1	At the end of Week 3
Severity of Joint Pain	2.10 0.75	1.30 0.77**	0.35 0.56***
Morning Stiffness	2.07 0.90	1.51 0.79**	0.59 0.66***
Functional Disability	1.87 0.81	1.53 0.91*	0.84 0.76**

* *P NS - Not Significant*

** *P < 0.05 - Significant*

*** *P > 0.001 Highly Significant*

Global Assessment

A global assessment of the patients on the 4 points scale mentioned, at the end of 3 weeks showed that in 90.52% of the patients the response was excellent to good, fair in 6% of the patients and poor in 3.48% of the cases respectively (Table 6). However, individual case assessment showed that pain relief to some extent or the other was seen in almost all cases.

Laboratory Investigations

RF was positive in 75% of the RA cases i.e., 24 cases out of 32. ESR was raised (>25 mm/for Ist hour) in 80% of all cases enrolled i.e. 48 out of 60. UA was raised (>7 mg/100 ml) in only 8 cases out of 60 i.e. 13.3%. At the end of the 3 weeks period no significant change was seen in the RF status but ESR showed a significant decline (Table 6) and interestingly in all cases of raised UA (Gout) the values showed a downward trend.

Table-6: Effect of EazMov Plus on Erythrocyte Sedimentation Rate (ESR - Wintergreen's Method) after 3 weeks Treatment

ESR > 25 mm For Ist hour in 48 out of 60 cases (80%)	
Mean ESR Value ± SD at Beginning of Treatment (mm fall for ISt Hour) (Day Zero)	Mean ESR value ± SD at end of 3 weeks (mm fall for Ist hour)
90 20.2	20 4.5

Table-7: Global Assessment of Patients at the end of Treatment

Assessment	% of Patients
Excellent / Good	90.52
Fair	6
Poor	3.84

Side Effects

Three percent i.e. 5 cases out of 60 complained of adverse events which were mainly nausea, anorexia, abdominal discomfort and abdominal pain. All side effects were mild and did not warrant discontinuation of treatment, and were relieved spontaneously.

Discussion

This study highlights the beneficial role of "EazMov Plus" in arthritides of diverse aetiology with results similar to NASIDs[12]. Earlier studies have established the Gastrointestinal friendly and safety profile of this formulation[11]. The significant improvement in pain (75.3%), reduction of inflammation (78.7%) and 68% improvement in joint function more than fulfill the criteria laid down for an ideal antiarthritic drug as outlined by American Rheumatological Association[1-3,13]. The previously documented anti-inflkammatory and analgesic properties of this formulation in laboratory animals against different arthritic models are amply borne out in the current study also, as shown by the significant improvement in non-specific parameters such as ESR. This effect was seen in all types of cases where ESR was raised irrespective of the nature of the arthritis[9,10].

Relief in RA could be due to the effect of this formulation and its various ingredients[14]. Interestingly in a small percentage of patients where Serum Uric acid was raised it showed a tendency for normalization thus bringing out the beneficial effect of this herbal antiarthritic in gout. However, wider and planned trials in such patients are required to bear this out. Safety of the product is once again proved.

This multicentre COMP shows the beneficial effect of "EazMov Plus" in RA, OA and NSA and proves the immense benefits that can be obtained with the use of this herbal formulation in "Real Life" clinical situations.

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CURRENT STATUS OF PASSIVE TUBERCULOSIS DETECTION IN A RURAL DISTRICT OF J&K

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Abstract: Tuberculosis affects one fifth of the mankind and kills more people than any other infectious disease, yet misdiagnosis and under-reporting is rampant. The situation in rural areas is especially disappointing. Despite decades of a national level programme for control of tuberculosis no improvement has occurred in detection and reporting. Analysis and comparison of the records of the DTC of a rural district has shown almost no improvement in the dismal performance over the last full decade. The failure of passive detection of cases, especially the bacillary positive cases, has suggested that active detection coupled with epidemiological investigations are needed to boost the routine case detection and to find out the bottleeks in the implementation of the National Tuberculosis programme in rural areas.

Tuberculosis is one of the oldest of human diseases which has spared no civilization, race or nation. India currently has 14 million TB patients[1] and of the 3.5 million new cases reported from the Southeast Asia in 1998, 2.3 million (65.7%) were contributed by India[2]. TB kills one in India every minute and during that 1 minute 60 persons get infected from one infectious (sputum positive) case. Estimatedly there are 3.5 million sputum positive cases in the country and each such case infections at least 10-15 persons every year[3]. This shows that control of tuberculosis in India, as elsewhere in the developing world, has necessarily to focus on the infectious pool to which 1 million cases are added annually[4].

Tuberculosis, affecting one fifth of mankind and claiming more lives than any other infective disease, has rightly been called the biggest public health problem in India. Yet it remains a generally misdiagnosed and underreported disease because of various reasons and our state is no exception. Gross under-diagnosis & rare reporting is universal but the problem is worse in rural areas. To assess the efficiency and efficacy of TB detection and reporting in a typical rural district (Pulwama) we retrospectively analysed the D.T.C., records of the year 1998 (Jannuary to December), and to have an idea of decadal change compared the results with those for the year 1997-98 (October 1997 to September 1998). Pulwama, a rural district is located at a distance of 40 km from Sriagar, the summer capital of J&K State. The 1998 profile of the district, based on the 1981 census, is reproduced in Table-1[5,6]. The comparative figures for 1998 were not available since no census was held in J&K in 1991 and the current total populaltion is a projection by the Directorate of Health Service Kashmir used in TB statistics.

The population as evident is primarily rural, engaged mainly in cultivation and farming, with a literacy rate that is lower tha the State average of 26.17%. Population density is 289 which is the highest for any rural district of Jammu or Kashmir Division. The male - female ratio is same as the State average and quite similar to that in other districts of the valley. Geographically the district consists of a terrain that should not pose any special problem in health care delivery (preventive, promotive or curative). No area is difficult to reach, cater or monitor, and a reasonable vicinity to and congruence with the Capital city makes it an ideal district for evaluating impact of various health care schemes, projects and programmes.

Analysis of the data reveals that a total of 169 cases of TB were registered during 1998, of which only 5.3% were sputum positive; the bulk belonged to x-ray positive (63.3%) and extrapulmonary cases (31.4%). The respective percentages for 1998 were 7.3, 56.2 and 36.5% (total cases 329). Total disease detection rate was 0.42/1000 in 1998 which increased to a marginal 0.55/1000 in 1998 when adjusted for the projected district for 11998 was 811 cases (1.34/1000) which was less than the nationally expected prevalence of 4/1000. The rate of detection of sputum positive cases doubled from 0.02 to 0.04/1000 over the decade and that for the extra-pulmonary cases increased from 0.13 in 1988 to 0.20 per 1000. This was much lower than the national target of 1.3/1000 new bacillary cases annually. (Table II)

Age-based analysis indicated that only 23 cases of tuberculosis were detected in the under 15 year age group in 1998 as against 37 a decade back. This decrease was

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Table-I Description of the Studied District (Pulwama) *1998

Total area	1,398 sq km.
Population	4,04,078
Populaltion density	289/sq km
Males/Females	52.72% / 47.28%
Sex ratio M/F x 100	112
Profession	Cultivators 19.03% Agricultural Labour 0.59% Marginal workers 21.66% Others 9.42% Non-workers 49.30%
Literacy rate	20.47%
Health facilities:	Primary health centres 10 Subcentres 66 ADS 30 UDS 22

The figures relate to the 1981 Census and are applicable as on March 1998

Table-II: Comparative Descriptive Data (1988 & 1998)

Descriptive Class	Sputum +ve		X-ray + ve		Extra-pulmonary	
	1988	1998	1988	1998	1988	1998
I) Age group						
< 15 yr M	0	0	10.28	3.78	15.10	0
F	0	0	14.00	2.70	5.66	9.18
15-20 yr M	0	16.67	2.80	4.86	1.89	5.0
F	11.11	0	5.60	8.11	1.89	7.5
21-30 yr M	33.33	25.00	6.54	14.60	5.66	10.8
F	0	4.17	11.22	11.35	7.55	11.67
31-40 yr M	0	4.17	2.80	9.19	13.20	5.84
F	0	12.5	11.22	9.73	11.32	9.18
41-50 yr M	11.11	4.17	6.54	5.40	1.89	5.83
F	0	12.5	7.48	6.49	15.10	8.33
51-60 yr M	11.11	0	9.35	4.32	3.77	4.17
F	33.33	0	2.80	4.86	7.55	8.33
61-65 M	0	4.17	2.80	2.70	0	2.5
F	0	4.17	0	2.16	1.89	1.67
> 65 yr M	0	4.17	4.67	5.95	1.89	7.5
F	0	8.33	1.87	3.78	5.66	2.5
All males	55.56	58.33	45.80	50.82	43.40	41.67
All females	44.44	41.67	54.20	49.18	56.60	58.34
Total	100.00	100.00	100.00	100.00	100.00	100.00
II) According to place of residence:						
- Rural	100.00	100.00	(Not know)	97.84	(Not known)	98.33
- Semi-urban	–	–	–	2.16	–	1.67
- Unmarried	–	–	–	–	–	–
III) Martial Status:						
- Married	100.00	62.50	63.55	78.38	79.25	77.50
- Unmarried	0	37.50	36.45	21.62	20.75	22.50
IV) According to Profession:						
- Students & Jobless	(Not know)	(Not know)	31.78	13.51	18.87	16.67
- Farmers	(Not know)	(Not know)	42.05	44.33	20.75	15.83
- Housewife	–	–	21.50	32.97	45.28	15.83
- Others	–	–	4.67	9.19	15.09	7.50
V) (All figures are in percentages)						

evident primarily in x-ray positive cases, since no sputum positive cases occurred in that group and the extrapulmonary cases showed no change. The 15-30 year age group showed a two fold increase in x-ray positive cases ad 3-fold increase in detection of extra-pulmonary cases. No appreciable change was seen in the past-30 year age group except in the past fifty group which manifested in increase in extrapulmonary cases (Table II). Sexwise analysis showed that in 988 females accounted for 54.4% cases which decreased slightly to 51.9% in 1998. The males and females did not differ in detection rate in any of the 3 categories in 1988 but twice as many sputum positive males were registered in 1988 as females. Other categories, however, showed no change in detection rate over the decade (Table III).

Table-III: Decadal Changes in Detection of Cases

Category	1988		1998		Detection rate/ 1000		Decadal change (1988-98, %)
	No.	%	No.	%	1998	1998	
Sptum +ve							
Total	9		23		0.02	0.04	+200%
Males	5	(55.56)	14	(60.86)	0.03	0.03	+300%
Females	4	(44.44)	9	(39.14)	0.01	0.01	Nochange
X-ray +ve							
Total	107		185		0.26	0.31	+119.23
Males	49	(45.80)	94	(50.82)	0.12	0.16	+133.34
Females	58	(54.20)	91	(49.18)	0.14	0.15	+107.14
Extrapulm. T	53		120		0.13	0.20	+153.85
onary M	23	(43.40)	50	(41.67)	0.06	0.08	+133.34
F	30	(56.60)	70	(58.33)	0 .07	0.12	+171.42
All T	169		328		0.42	0.55	+130.95
M	77	(45.56)	158	(48.17)	0.19	0.26	+136.84
F	92	(54.44)	170	(51.83)	0.23	0.29	+126.09

In 1988 only 32% cases were enrolled directly by the District Tuberculosis Centre (DTC) Pulwama; in 1998 this proportion reached in 62%. While 70.4% of patients were unmarried in 1988 in 1998 this percentage (76.9%) showed a slight increase. The 1998 figures revealed that the vast majority of cases were rural. The records, in 1988 as well as in 1998, were largely incomplete and could not yield any other epidemiologically useful information.

Discussion & Conclusion:

Tuberculosis which was showing a descending secular trend all over the globe resurfaced as a major public health problem mainly because of the development of resistant bacterial strains and increased prevelence of HIV infections[7]. With a 38% prevalence of infection and 0.4% prevalece of sputum positive cases. India is identified as a country of high transmission and inadequate decline[8]. There are 3 to 4.4 millio bacillary cases in the country each of whom will potentially will eventually develop some form of clinical tuberculosis[9,10]. Each year 3-5 lakh people will continue to die of TB in India during the coming many years. Studies have shown that patients are not exposed only to the direct mortal effects of TB but their mortality from other diseases also is higher for many years after the attack of TB[11]. Morbidity, inconveience to the patient and his family, and economic costs to the nation, society and family are overwhelming. Research has revealed that when a mother dies, her children suffer high rates of mortality[10]. Gross underdiagnosis, as is the case everywhere in the J&K State, means that large number of tuberculosis patients are being missed with all social, economic and cultural consequences of chronic ill-health and subsequent death, and worst still missed infectious (bacillary or sputum positive) cases continue to infect and reinfect unsuspecting masses and continue to keep the infection simmering in the community. This also needs to be kept in mind that case fatality rate in untreated bacillary cases is as high as 14%[4].

In 1998 the DTC Pulwama was able to detect a mere 329 patients against the target of 811 (40.5% an achievement). Against a given target of 1472 sputum tests 1841 sputa were microscopically examined for acid fast bacilli but only a total of 23 positive cases were picked. With a population of 601414 (which is the lowest projection) Pulwama district is expected to have a minimum of 1200 sputum positive cases with each of its 600 odd villages having 2-3 such cases and 8-12 radiologically positive cases at any point of time[12]. Extreme under-diagnosis, thus, is quite evident. Other districts also can not bost of any better performance. Overall the performance in our study district has been so poor and erratic that no conclusions of epidemiological significance were possible. Pulwama is, in fact, the weakest district as regards TB detection and reporting, and has shown that passive case detection has not improved over the last 10 years. An evaluation survey may help to assess various factors behind the poor performance of National TB Control Programme, and active case detection may have to be started to boost the passive detection in the lagging areas.

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CSF RHINORRHEA - DETECTION BY TC-99M DTPA CISTERNOGRAPHY

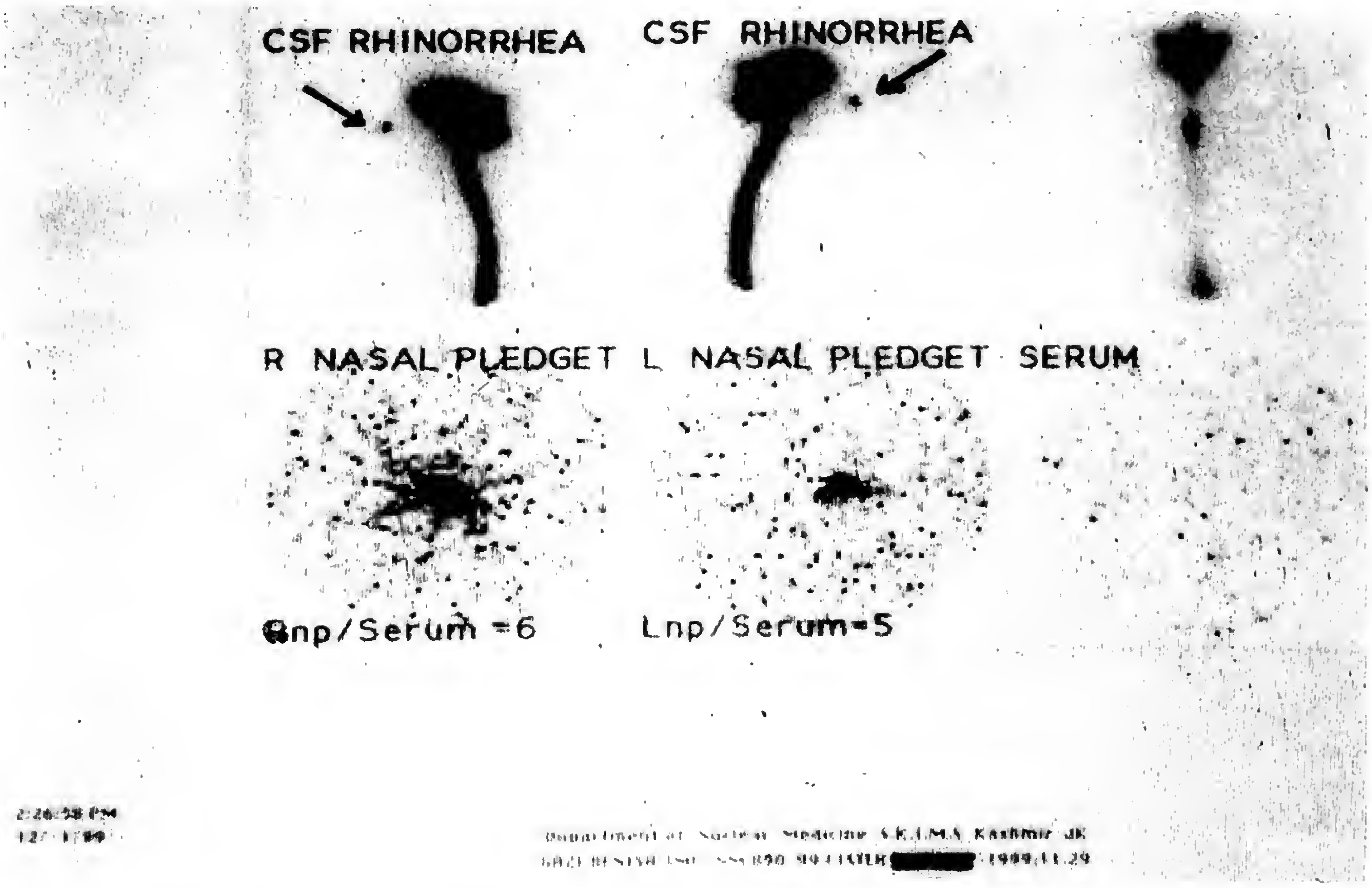

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Fig. 1: CSF Rhinorrhea detected by Tc-99m DTPA scan, showing the site of leak and a high nasal pledget to serum ratio

A three year old male child was admitted in the department of Neurosurgery, SKIMS with eighteen days history of fall from a height of about 10-12 feet. He had immediate nasal bleeding and a single bout of vomiting. At admission he was fully conscious and co-operative. General and systemic examination was unremarkable. A contrast enhanced CT scan of head was reported normal. However, the child continued to have continuous watery discharge from the nose which initially was thought to be due to coryza but later a possibility of CSF rhinorrhea was contemplated and a Tc-99m DTPA scan was advised 10mci of Tc-99m DTPA was injected intrathecally followed by a flush of 15ml of sterile saline. Nasal pledgets were placed in both the nostrils. After 4 hours of injection both the nasal pledgets were removed and counted for radioactivity. Blood sample was obtained at the same time and allowed to clot and 0.5ml of serum was also counted for background activity. Bilateral CSF rhinorrhea was established by a high right nasal pledget (Rnp) to serum ratio of 6 (normal=1) and also a high left nasal pledget (Lnp) to serum ratio of 5 (normal=1). The CSF leak in the nasal cavity was also evident of the 4 hour image acquired on Siemens Icon LFOV gamma camera. Tc-99m. DTPA cisternography is a very sensitive investigation for diagnosing CSF rhinorrhea.

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ACE INHIBITORS AFTER MYOCARDIAL INFARCTION

Therapy with Angiotensin Converting Enzyme (ACE) inhibitors is now an integral part of infarction management. The status of these drugs has been achieved after thorough analysis of the ACE inhibitor trials, many of which have been large and multicenter. The following is a brief description of the important trials pertaining to the subject that could prove handy and refresh the knowledge of both physicians and cardiologists.

The first significant trial demonstrating beneficial effect of ACE inhibitors during MI was " Survival and Ventricular Enlargement (SAVE) study (1,2). This study randomised 2231 patients with MI (confirmed acute MI, 3 to 16 days old) to Captopril (forced titration to 25mg TDS) or placebo if LVEF was <0.4 on radionuclide ventriculography. It was observed that there was 22% risk reduction in death and similar reduction in morbidity in addition to the benefits obtained with aspirin and beta blockers.

The AIRE (3,4) " Acute Infarction Ramipril efficacy " study randomised 2004 MI patients with clinical or radiological signs of heart failure (not requiring ACE therapy) to Ramipril (target dose 5mg BID) within 10 days post MI (mean 5.4 days). The average follow up was 15 months. It was seen that Ramipril therapy reduced the risk of death by 27% and CHF or progression to severe CHF was also significantly reduced showing that the high risk infarct population is particularly benefited by ACE inhibitor therapy.

In the TRACE (5-7) "Trandolapril Cardiac Evaluation" study, 1749 patients were randomised to receive either Trandolapril 2mg or placebo within 7 days of acute MI with wall motion index <1.2 (approximates to LVEF <0.35). This study confirmed the findings of SAVE and AIRE showing marked reduction in mortality in patients with low EF.

SMILE (8) " Survival of Myocardial Infarction Long-Term Evaluation" study randomised 1556 non-thrombolysed MI patients to Zofenopril to a target dose of 30mg OD or a placebo within 24 hrs of admission. The study showed that this high risk group fears better in terms of severe CHF and mortality with early ACE inhibition, a 22% reduction in mortality.

GISSI-3 (9,10) ; third Gruppo Italiano per lo Studio de la Sopravvivenza infarcto myocardio randomised 19,394 patients to Lisinopril, 10 mg or placebo to MI patients admitted within 24 hrs of onset of pain. It showed that patients in Killip II or more at baseline had maximum benefit and 28% lives are saved in first 24 hrs suggesting therapy should start at admission.

ISIS-4 (11-13) " Fourth International Study of Infarct Survival" randomised 58,050 patients to Isosorbide mononitrate or captopril or magnesium in a 2/2/2 factorial design within 24 hrs of the onset of pain. In this study only modest mortality reduction and no significant morbidity reduction was observed possibly because of higher number of low-risk patients.

CONSENSUS-II " Cooperative New Scandinavian Enalapril Survival Study" (14) studies 6090 patients by randomising them to enalaprilate I/V by infusion followed by oral enalapril after 6 hrs or placebo. This trial showed a statistically insignificant increased mortality in the treated group possibly due to hypotension caused by early aggressive therapy.

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To be concluded

EPILEPSY AND PREGNANCY

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Epilepsy is amongst the most common disorders treated by neurologists and is one of the frequent serious neurological conditions encountered by obstetricians. It effects 0.5% of women of child bearing age[1]. Considerations for patients with seizure disorders who desire pregnancy include the effect of pregnancy on the control of seizures, the fetal risk associated with maternal seizures and teratogenicity of anticonvulsant drugs. In the past 20 years advances in genetic epidemiology, emergence of new anticonvulsants and advances in surgical techniques have permitted more than 75% epileptics to live with little interference from seizures. Inspite of these advances, epileptic women and their newborns continue to be at risk for a variety of complications of pregnancy (Table I). Of all women with epilepsy, 13% have their first seizures during pregnancy, and 40% of these women have seizures only during pregnancy. Multiple factors may contribute to alteration in the frequency of seizures during pregnancy. Explanations include hormonal and metabolic changes associated with pregnancy, altered distributions of anticonvulsant medication, non-compliance, psychological stress, physical fatigue and maternal sleep deprivations[2,3].

The objectives of treatment of pregnant women with epilepsy are to maintain the patient in a seizure free state, minimize the adverse effects of seizure disorder on pregnancy and reduce the teratogenic effects of anticonvulsants on foetus. Drug regimens and dosage schedules require modification to achieve this. The description to follow focuses on the management of epilepsy in these special circumstances.

Etiology of Seizures during Pregnancy:

Most of the women who present with epilepsy in pregnancy have no demonstrable structural lesion. Tumors are a rare cause of seizures in women of reproductive age group but some epileptogenic tumors such as meningiomas may rapidly increase in size during pregnancy. Similarly arteriovenous malformations may expand or undergo occlusion during pregnancy. Late in the pregnancy or early puerperium patients may develop cortical vein thrombosis with seizures.

Pregnant women with epilepsy can be divided into two categories, those described as having epilepsy before their child was conceived and in whom a level of seizures control has been established and those who experience a seizure disorder not related to toxemia for the first time during pregnancy. Fewer than one quarter of the women in the latter group will have seizures only during pregnancy; the term "gestational epilepsy" has been applied[2]. The occurrence of gestational fits in one pregnancy does not suggest that they will recur in subsequent pregnancies.

Most studies suggest that approximately 50 percent of whom with epilepsy will have no change in their seizure frequency while pregnant, 40 percent will have more seizures than before and 10 percent will have seizures. In one of the most recent of these studies Schmidt et al have prospectively monitored the effect of pregnancy on seizure frequency in 136 pregnancies in 122 epileptic women[3]. In 50 pregnancies (37 percent) the number of seizures increased during pregnancy or in puerperium. In 34 of these (68 percent) the increase was associated with non-compliance with treatment regimen.

The influence of specific hormonal changes on the nervous system has been considered a mechanism that could alter the frequency of seizures during pregnancy. In animal studies oestrogens and chorionic gonadotrophins seem to lower the seizure threshold whereas progesterone may raise this threshold[4]. This correlation has not been shown in humans nor have fluctuating hormone levels been correlated with catemenial epilepsy or seizures occurring principally during menses[5].

Complications of Pregnancy

There are no differences between women with epilepsy and controls in the incidence of hyperemesis gravidarum or abruptio placetaie[6]. Bleeding at delivery may be increased because of Vit. K deficiency, produced by phenytoin, phenobarbitone primidone and other related compounds. Induction of labour and interventions during delivery are reported more frequently in epilepsy[7].

Toxemia is found in about same frequency in epileptic women in controls but the severity of toxemia is more in

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epileptics. Incidence of family history of seizures, EEG abnormalities and recurrent fits during pregnancy is higher among women with eclampsia. Whether toxemia is just a triggering factor in patients with primary cerebral dysarrhythmia or an independent syndrome is to be established.

Seizure and Outcome of Pregnancy

Overall pregnant women with epilepsy have twice the incidence of unfavourable outcomes in comparison with general population with respect to fetal viability[8]. Still births, microcephaly, mental retardation and non-febrile seizures occurred with increased frequency in the offsprings of women with seizure disorder[9]. Low birth weight, neonatal seizures and first year deaths were not increased in the offsprings of epileptic women. Generalised motor seizures especially when prolonged may compromise the fetus because of hypoxia and acidosis. The risk of epilepsy in children of parents with epilepsy is higher than that in general population. This risk is higher (relative risk of 3.2) only for children of mothers with epilepsy. Paternal epilepsy appears to have no impact on the development of seizures in children[10]. The presence or absence of seizures during pregnancy does not affect the development of seizures in the infant. Further evidence to support a genetic component for seizure development in these infants comes from kindling studies in experimental animals. If rats with experimental epilepsy are made to have generalised seizures during pregnancy, their offsprings are not more susceptible to kindling than are rats with no seizures during parturition[1].

Anti-convulsant Drugs and Pregnancy

Mygind et al, Launder et al and Hooper and Colleagues reported a decline in plasma level of anticonvulsants during pregnancy when maintenance dose was constant[12-14]. The available data suggest that phenytoin, carbamazepine and phenobarbital are cleared more rapidly from plasma during pregnancy[6]. For carbamezepine and primidone accelerated metabolism may be in part responsible, for phenytoin, the data are less clear[6].

Anticonvulsant drugs are transferred across the placenta and rates of placental transfer and fetal elimination are known for phenytoin, phenobarbital, primidone and carbamezepine[2,14]. Phenytoin concentrations are identical in cord and maternal serum at term[15]. The half life of phenytoin in the plasma of new born ranges from 55 to 69 hours. Elimination of the drug by the fetus is generally completed by fifth day. Phenobarbital concentration in human umbilical cord plasma are virtually identical to those in maternal plasma. Phenobarbital is eliminated from newborns within two to seven days; infants born of epileptic mothers may be dependent on phenobarbital and may experience withdrawal symptoms which are characterised by hyperexcitability, tremor, restlessness and difficulty in sleeping but not seizures[6].

The half life of carbamazepine in the new born ranging from 8 to 28 hours, is not significantly different from half life of drugs in adults[7].

Despite these facts breast feeding should not be discouraged unless the infant suckles poorly and is somnolent, in which case early wearning can be considered.

Teratogenicity

All women with epilepsy who wish to become pregnancy should realise that most anticonvulsants have been implicated as teratogenic and risk of congenital malformations among infants born to epileptic women is greater than the general population. The risk factors which have been emphasised are the inherent teratogenicity of anticonvulsant drugs, the occurrence of frequent convulsions during pregnancy increased incidence of complications during pregnancy and lower socioeconomic status[8]. Bjerkedel ad Egennaes[7] reported that incidence of congenital malformations in babies born to epileptic mothers was 1.25 times higher than controls.

In a multiinstitutional study 657 pregnant women with epilepsy were studied[19]. The incidence of congenital malformations was lowest in mothers who remained free of seizures and unmedicated during pregnancy (1.8%) next lowest in mothers who remained free of seizures and took medications (11.5%) and highest in those having seizures and taking medication (12.7%). Cleft plate, ceft-lip and cardiac defects are the most frequently seen congenital anomalies in those patients. There specific syndromes have been reported in association with phenylhydantoin, trimethadone and valproic acid. Foetal hydanatoin syndrome is characterised by broad nasal bridge, low set ears, hyperteleorism, epicanthal folds, digital hypoplasia, intrauterine growth retardation and mental retardation. Trimethadone is the most teratogenic anticonvulsant. The affected infants have low set ears, palatal anomalies, irregular teeth, v shaped eye brows and speech disturbances. Some infants have intrauterine growth retardation, short stature, cardiac anomalies, ocular defects, simian creases, hypospadias and microcephaly. Valproic acid is teratogenic and produces dose related morphological abnormalities in animals. There is a possible association between neural tube defects and valproic acid, foetal valproate syndrome has been reported recently[19]. It consists of craniofacial anomalies, e.g. epicanthal folds, flat nasal bridge, small anteverted nose, long upper lip, down turned mouth and thin vermillion border.

Seizure Therapy in Pregnancy

Patients with partial seizures, raised intracranial tension and evidence of focal neurological deficits need detailed evaluation as to their cause. An electroencephalogram is advisable in deciding the type of seizures but is unlikely to help in deciding the underlying etiology. Computed tomography is reqiured for diagnosing a structural lesion. This is reasonably safe for foetus which can be protected from scattered radiation by suitable lead curtain and abdominal screening. Magnetic resonance imaging is an alternative but should be avoided in early pregnancy. Epileptic women of child bearing age should be informed of the risks associated with anticonvulant use prior to conception. By the time most of these patients realise that they are pregnant, potential malformation may have already developed because of antiepileptic drug use. Such women who had been free of seizures for three years should have anticonvulsant drugs gradually withdrawn before planning pregnancy. In those who still require antiepileptics there should be an attempt to use the minimum possible effective dose of a single anticonvulsant drug which will provide effective seizure control. Carbamezepine or phenytoin should be employed for sustained treatment of primary generalised tonic clonic seizures, partial seizures with or without secondary generalisation and complex partial seizures. Carbamazepine is first choice as risk of teratogenesis is least with it and it has fewer side effects in the long term use. However, choice will depend on the familiarity of treating physician with the drug, socio-economic status and tolerance of patient. Trimethadone should not be used as it has been found to be highly terratogenic in a multicentre study[20]. Sodium valproate should be avoided as it is likely to produce neural tube defects. The dose of carbamazepine will range from 400 to 1200 mg per day, the average being 600mg per day. One third of usual maintenance dose should be given initially when the therapy is started in a previous untreated patient. It should be increased weekly over a period of three to four weeks until the mean daily maintenance dose is reached. Phenytoin can be administered as a single 900mg loading dose. The effective maintenance dose of phenytoin is between 300 to 400mg daily. If seizures persist inspite of high therapeutic plasma levels at steady state, the second choice antiepiletic drug is added and the first drug is gradually withdrawn when trough plasma levels of second drug reach the therapeutic range and seizures stop. If single drug can not control the seizures, they can be administered in combination. However, if seizures are not controlled by combination of two anticonvulsants, the addition of third drug is unlikely to change the scenario. Generalised tonic clonic status is a medical emergency and requires immediate hospitalisation. Absence seizures may rarely be seen during pregnancy. Ethosuximide is the drug of choice given in doses of 250mg three to four times daily. Clonazepam 1 mg three times a day may also be useful in controlling these seizures.

Long term antiepileptic medication in non epileptic women who develop eclampsia is not required. No prophylactic treatment is warranted for gestational epilepsy as recurrence of seizures in subsequent pregnancies is unpredictable[21].

Folate Supplementation

Treatment with antiepileptic drug may result in decreased serum folate concentration and occasionally megaloblastic anemia in pregnancy. There is no evidence that low folate concentration results in increased frequency of seizures. A low dose folate supplement is sufficient for pregnant women with epilepsy who are receiving concomitant anti-convulsant drugs.

Labour, Delivery and Birth

Most patients with epilepsy have a normal vaginal delivery[22,23]. Risks for mother and infant are present in the rare women whose convulsions or complex partial seizures continue to be intractable to treatment during the third trimester and often occur as weekly attacks, as seizures in clusters or status epilepticus. The threat of fetal asphyxia caused by repeated tonic clonic seizures or convulsive status epilepticus during labour might justify an elective caesarean section in such patients[24]. Prompt caesarean section should be performed when repeated tonic clonic convulsions can not be controlled during labour or when mother is unable to cooperate during labour because of impaired awareness secondary to seizures[22].

A tonic clonic seizures occurs during labour in 1 to 2% of women with epilepsy and 24 hours after delivery in another 1 to 2%. Maintenance of plasma antiepileptic drug AED levels known to protect against seizures during 3rd trimesterr is a preventive measure against the occurrence of seizures during labour. Taking AED during labour to ensure the adequate plasma levels is also important and patient must be cautioned against missing doses as labour continues[25].

Convulsive seizures during labor and delivery should be treated promptly and are best managed with intravenous benzodiazepines. Intravenous lorazepam has been suggested as drug of choice to stop repeated seizures during labor[25]. Disagreement continues as to whether phenytoin should be used to stop repeated convulsions during labour because phenytoin inhibits myometrial contractions and might prolong labour[26].

A majority of neurologists and obstetricians consider it prudent to administer vit. K1 (20mg/day) prophylacticaly to AED treated mothers during the last month of pregnancy as a means of protecting the infant against severe postnatal bleeding caused by deficiency of vitamin K1-dependent clotting factors II, VII, IX and X[27].

All newborns born to epileptic mothers should receive 1 mg of vit. K intramuscularly at birth as a prophylactic measure against the haemorrhagic disorder due to clotting factor deficiency as mortality from this postnatal bleeding disorder is high (>30%) because internal bleeding in infants is not noticed until the infant is in shock[28]. If clotting studies in such infants reveal abnormal levels, additional doses of vit. K may be required. Severe cases may require fresh frozen plasma or concentrates of factor II, VII, IX and X.

Breast feeding

Most of the mothers taking anticonvulsant drugs may safely breast feed their children. The concentration of anticonvulsants in breast milk is considerably low, the milk/blood ratio being 0.1 for diazepam and valproate, 0.6 for carbamazepine and phenobarbitone and 0.15-0.53 for phenytoin. Except for rare allergic reactions and sedation with phenobarbitone and diazepam due to slow metabolic rate in neonates, no untoward effects are reported. In practice, carbamazepine, valproate and phenytoin have little clinical effects on neonate.

Table-I: Risks of pregnancy for epileptic women on anticonvulsants

Type of risk	%age
Incrase in seizure frequency	24 - 32
Vaginal bleeding	5
Malformed child	11-12
Neonatal haemorrhage	10
Spina bifida (on valproate)	1

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MRI-EVALUATION OF SPINAL PATHOLOGY

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Introduction

The spine is the region of the central nervous system where magnetic resonance ultimately is likely to have its most significant impact. Currently, imaging of the spine is the second most commonly performed MR examination following studies of the brain. There has been considerable interest in the role of MRI of the spine with respect to other imaging modalities during the past several years. In 1984, reports began to appear indicating that MR was potentially more useful than CT in examining certain areas of central nervous system, especially the brain.

At the present time, with continuing tenchologic advances for MR and a relatively static technological environment for CT, the advantage continues to shift towards MR. As we advance towards the end of this decade, most investigators would agree that MR rather than CT is becoming increasingly the examination of choice in many clinical situations for the spine as well as for the brain.

Principle of MRI

Certain atomic nuclei, which possess unpaired protons and neutrons, possess an inherent spin. The nucleus is positively charged and therefore creates a small magnetic field around it when it spins. The human body contains copious amount of water and is therefore rich in hydrogen which fortunately, possesses the required magnetic quality.[1]

When the tissue containing these nuclei are placed within a strong magnetic field, the nuclei tend to align themselves along the line of force of this field. The spinning protons now tend to preces i.e. wobble about the axis of the main magnetic field. Now, a radio frequency pulse is applied, being of the same frequency as the precessing nuclei but at right angles to the main magnetic field. This excites the protons, at low energy levels, into higher energy states. Thus, an absorption of energy is taking place, which is released as the exciting protons relax back to their original energy level when the radio-frequency is switched off. The relaxation of the protons back to their original energy state is exponential in character and is called the spin lattice or T1 relaxation time. When the radio-frequency is applied the proton precess in phase. However, during the relaxation, they get out of phase due to small variation in magnetic fields. This is called the spin-spin or T2 relaxation time. Depending on the type of tissue under study T1 and T2 relaxation time will differ, thus giving rise to the difference in the images.

The MRI image depends upon four main factors:

1. The T1 relaxation time
2. The T2 relaxation time
3. The proton density
4. The blood flow

Depending upon the characteristics of the above four parameters, the signal intensity of the images will vary, thus deciding the appearance that any given tissue will finally cast.

Advantages of MRI

- It is non-invasive.
- Does not involve the use of ionizing radiation.
- It gives high intrinsic contrast.
- Without changing patient position, the images can be contructed in almost any desired plane.
- It has no currently known biological hazard.

Disadvantages of MRI

- The imaging time is long, hence patient motion artifacts are possible.
- Requiring expert technical staff.
- It is extremely expensive
- Bone can not be imaged
- Patient with pace-makers and other ferromagnetic implants can not be scanned.

Contrast Agent:

Gadolinium: Gd-DTPA is currently the only intravenous MR contrast agent approved for routine clinical use. In humans it has a plasma half-life of 90 minutes and more than 90% of it can be recovered in the

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urine within three hours following the administration.In more than 7000 clinical studies to date,no fatal reactions have been associated with the Gadolinium.Minor reactions like headache,local burning,urticaria are there.

MR Imaging Technique and Anatomy

Thin high resolution MR images are required to evaluate the spine,especially for the cervical region.Specially designed surface coils matching their sensitivity of depth and coverage to the region of interest are required.Spin echo-pulse sequence with a short TR (200-4000 msec) and short TE (20-25 msec) should be used to obtain the T1 weighted images of the spine.Long TR (2000-4000) with long TE (50-100 msec) should be used to obtain T2 weighted spin echo-images.Proton density images with a TR of 2000-4000 and TE of 20-25 should be included as the first echo of a dual echo squence.3 mm slice thickeness 60 or 20 cm field of view,2-4 excitations and 256x256 matrix are preferred.

On T1 weighted images,the spinal cord has an intermediate signal intensity that contrast with the low intensity of CSF.In this sequence the cortical bone has a negligible signal intensity that contrast with the higher signal intensity of fat containing bone marrow.The ligaments have intermediate signal intensity and the intervertebral disc has a nearly homogenous,low to intermediate signal intensity.

On T2 weighted images,CSF manifests a high signal intensity.The spinal cord has a lower signal intensity than CSF.Fatty bone marrow has a lower signal intensity than in T1 weighted images.Fibrocartilage in nucleus pulposus and central portion of annulus fibrosus on T2 weighted images has a high signal intensity,whereas the peripheral collagenous portion of the annulus fibrosus has a low signal intensity.

Proton density images have been less commonly used in clinical spine imaging although the intervertebral disc,the ligaments,CSF and to only a limited extent,the spinal cord are well demonstrated in these images.

Congenital Anomalies

Congenital anomalies like Arnold-chiari-mal formation,spinal dysraphism, meningocoele,tethering of cord and sacral lipomas can all be directly and accurately delineated using multisection imaging without the need for extensive invasive procedure.

Chiari-mal formations: This is characterised by dislocation of HIND BRAIN STRUCTURES into the spinal canal.[2]

Hydromyelia and Syringomyelia: Hydromyelia is defined as dilatation of central canal of the spinal cord and syringomyelia is defined as cavitation and cyst formation within the substance of the cord.[3]

On MRI the full extent of cavitation into the cord can be very well demonstrated.T1 weighted image does not show contrast enhancement,unlike neoplasm.

Simple Meningocoele: It is diverticulum of arachnoid and dura which protrudes through the posterior spina bifida into the dorsal subcutaneous tissue.It is nearly always covered by skin.[4]

Anterior sacral Meningocoele: It is an anterior herniation of meninges through a congenital defect in the sacrum or coccyx to form a CSF fluid filled hernial sac.Hyper-intense CSF within anterior sacral meningocoele can be demonstrated.

Spina Bifida Aperata: It is of two types Myelocoele and Meningomyelocoele.

Meningomylocoele patients are born with an oval plate of moist,reddish neural tissue exposed on the midline of back.This plate is surrounded by a variably epithelialized zone of meninges which connects the plate with the surrounding skin.In this condition,expansion of the CSF fluid space lifts the plate and meninges above the level of surrounding skin.[4]

In Myelocoele,the plate and meninges lie flush,with the rest of the back.

Tight Filum Terminale Syndrome is caused by tethering of the spinal cord by a thickened filum terminale which may be thickened by lipomatous or fibrous tissue.The normal location of conus medullaris can be as low as the body of L3 in newborn and infants (more than three months age).

T1 weighted image will demonstrate the high signal of enlarged filum if it is due to fatty infiltration.If it is thickened by fibrous tissue it will be iso-intense with the spinal cord.

Diastomatomelia: is characterised by partial or complete sagittal clefting of the spinal cord.T1 weighted MR images are good for demonstrating the clefting of the cord and other associated anomalies like hydromyelia.(5)

Infections and Inflammations

Acute myelitis produces swelling of the spinal cord and increased signals over several segments on T2 weighted images.

Diskitis and Osteomyelitis: Show low signal in vertebral bodies.There is thinning and disruption of the normal low signal band of the cortical bone of vertebral end plates.There is decrease in disc space height and persisten abnormal signal in vertebral bodies.The better defined hypo-intense line at inferior margin represents reactive bony sclerosis as part of healing process.

Multiple Sclerosis: T2 weighted sagittal image reveals multiple hyper-intense foci in the cervical spinal cord and the lower medulla.[6]

Degenerative Diseases

Disc degeneration is accompanied by loss of water content and therefore,signal intensity on MR images.The traditional findings of decrease in disc height and presence of calcification and gas assist in diagnosing this condition.

The terminology for describing abnormal discs can be quite confusing and include a long list such as degeneration,bulge,protrusion,herniation,prolapse,extrusion, sequestration and free fragment.

Disc degeneration: refers to the biochemical and structural changes but the term is also used to refer to disc disease as a whole.

Bulging disc: enlarges circumferentially in a symmetrical fashion,subtle annular tear may be present but there is no major disruption of the annulus.The term protrusion and bulge are inter-changeable.But protrusion is the preferred term,it is eccentric to one side,indicating that the nucleus pulposus is begining to dissect through the annular fibers and thin the annulus.[7]

Herniation of disc: implies rupture of annulus with extrusion of nucleus pulposus through the defect.The extruded protion remains connected to the parent disc. Disc prolapse: is used to describe a herniated disc,covered by a few remaining annular fibers.

Perhaps,a disc prolapse could also be called a severe protrusion.

Sequestered disc: is a free fragment of disc material that is no longer attached to the parent disc.Free fragment can migrate above or below the disc space.

On T1 images a herniated disc generally has the same signal characteristics as the parent disc and is such as an extrusion of disc material into the spinal canal.[7]

Spondylosis: It can take the form of marginal end plate osteophytes or facet joint disease.When marginal osteophytes form along the vertebral end plates,the posterior longitudinal ligament is pushed posteriorly.Since the outer fibers of the disc annulus are attached to the posterior longitudinal ligament,the disc is also pulled posteriorly,resulting in a disc sandwich with the disc in the middle and the end plate osteophytes above and below.

Spinal stenosis: When bulging discs,spondylosis and ligamentum flavum hypertrophy progress to constrict the spinal canal and spinal stenosis develops.

Bulging disc,osteophytes and ligamentum flavum give a hourglass configuration (constriction of spinal canal at multiple levels).

Neoplastic Disease

MR imaging is the single most effective modality for the evaluation of spinal neoplasms by virtue of its ability to image the spinal cord directly and non-invasively.Mass lesion can be localized relative to the spinal cord,in conjunction with the patient's clinical history.It is thus possible to provide a brief,yet accurate differential diagnosis.Intravenous paramagnetic contrast enhancement also may prove extremely useful in further deliniating such lesions.In addition,it has demonstrated a high sensitivity to primary and secondary tumors of the bony spine through its ability to detect subtle T1 signal changes in the vertebral marrow space.

The annual incidence of primary spine neoplasms has been estimated at 2.5 per 100,000 per year.There is no significant sex-difference for the development of spinal neoplasia.

In a review of 4885 adult spinal cord tumors,presented in the literature,Nittner found neurilemomas 23% meningomas 22% glial (intra-medullary) tumors 13.2% and (extra-medullary ependymoma 2.5% sacroma 8.2% and metastasis 6% to be most comon.The remaining 25% of cases were dispersed among a wide variety of miscellaneous mass lesions.

Extra-dural: Chordoma,Haemangioma,Aneurysmal bone cyst, Metastasis,Sarcoma.

Intra-dural

1. Extra-medullary:
   Meningioma,Nerve sheath tumor,Metastasis, Neurofibroma,Dermoid,Epidermoid,Lipoma, Ependymoma also intra-medullary.
2. Intra-medullary:
   Glioma-Astrocytoma,Ependymoma,Glioblastoma,
   Dermoid,
   Epidurmoid
   Lipoma
   Haemangioblastoma,Metastasis.

On T1 weighted images,expansion of the cord is the hallmark of intra-medullary neoplasm. Gd.DTPA enhances areas of blood brain barrier breakdown to help detect characterise and define the extent of intramedullary neoplasms.

Focal areas of either increased or decreased T1 may be present within the expanded parenchyma owing to the presence of cysts or necrotic cavities.

Extra-Dural Neoplasms

Extra-dural tumors are comprised of primary or metastatic,benign and malignant neoplasms involving vertebrae,soft tissue,nerve roots and dura.These lesions account for approximately 30% of all spine neoplasms.

Chordoma:

Chordoma are uncommon lesions of bony spine arising from the remnants of the primitive notochord.They account for 3-4% of all primary bone tumor.Chordomas characteristically are found in the sacrococcygeal area (50%) with 30-40% arising from the basisphenoid and remainder from vertebral bodies.[8]

Sacral Chordoma is a soft tissue mass extends in to the pelvic cavity.The tumor is hypo-intense on the T1 image and hyper-intense on the T2 image.

Haemangiomas: Vertebral haemangiomas are slow growing benign lesions and are rarely symptomatic.They most commonly occur in the thoracic spine and have a distinctive appearance on MR scans.On T1 weighted images,the intra-osseous portion appear as mottled increased signal intensity secondary to the adipose tissue interspersed among thickened bony trabeculae.(8)

Aneurysmal bone cyst:

Like vertebral haemangiomas,aneurysmal bone cysts were thought to have a unique MR appearance.Comonly they manifest as expansile mass lesion with cyst containing blood and blood breakdown products bounded by thin periosteal membranes.MR imaging typically demonstrated nunerous well-circumscribed cystic cavities bounded by a low signal rim.

Intra-Dural Extra-Medullary Tumor

The largest single group of spinal mass lesions are extra-medullary intra-dural masses.Meningiomas are the commonest one.

Meningiomas:

Usually in older age group (above 40 years) more common in females.Rarely,meningiomas are both intra-dural and extra-dural.Sagittal and axial T1 weighted images typically demonstrate a small soft tissue mass within the spinal canal that is iso-intense to the spinal cord.T2 weighted images most commonly depict the tumor as a low signal (iso-intense with spinal cord) intradural defect surrounded by high signal CSF.(9)

Neurofibromas:

These tumors are seen most often in adults between the age of 20 and 50 years.They may occur any where in the spine with the thoracic spine being most often implicated.Majority of lesions are extramedullary.

T1 weighted image demonstrates an elongated hypo-intense mass in the ventral aspect of the spinal canal.Contrast enhanced scan reveal bright enhancement of tumor.[10]

Intra-Medullary Neoplasms

Gliomas:

Astrocytomas and ependymomas make up the overwhelming majority of gliomas.Ependymomas are often cited as the most frequent in adults,particularly as conus medullaris and filum terminale.They appear as a fusiform enlargement of spinal cord.

T1 weighted scans demonstrate expansion of upper cervical cord.The mass is heterogenous.Contrast Enhanced scans reveal enhancement.[11]

Haemangioblastomas: They are histologically similar to angioblastic meningiomas and apparently arise as small nodule from the pia.Sagittal scan shows cystic enlargement of cord.Tumour nodule enhances.Central non-enhancing area likely represents vascular pedicle of the haemangioblastoma.[12]

Metastasis:

Metastasis may also present as an intra-medullary mass lesion with nodular expansion.

The mass is iso-intense to the cord.Contrast enhanced scan demonstrates enhancement of the nodule.

Traumatic

The role of MR in spinal trauma has not been entirely defined.CT is used to detect non-displaced fractures of the vertebral arch,migration of fragments into the spinal canal,and associated herniated discs.MR has not made many inroads into the arena of acute spinal trauma because the examination takes longer,the image lack bone details.MR can certainly detect mal-alignment of the spine and major fracture of vertebral elements but can not match CT.MR can very well detect cord injury and epidural haematomas.The damaged cord is hypo-intense and has irregular,poorly defined margins.MR can also facilitate the diagnosis of delayed complications such as disc herniation.[13]

Post-Operative Spine

In the early post-operative period,interpretation of MR images is extremely difficult.The presence of fat graft,haematoma,gas and inflammation complicates the observed signal intensities.Moreover,recurrent disc and epidural scar exhibit similar signal characteristics (hypo- or iso-intense to disc on T1 weighted images and hyper-intense to disc on T2 weighted images).

After about one month,the acute post-operative changes resolve,making it easier to distinguish scar from disc.

Gd-DTPA should be used routinely in the post-operative back because it is valuable for differentiating the various post-opertative tissues.Epidural scar enhances to a much greater degree on MR than on contrast enhanced CT.The enhancing scar outlines any retained or recurrent disc fragments.A disc fragment induces a local inflammatory reaction,and vascular granulation tissue often forms about its perimeter.As a result,the perimeter of a herniated disc may enhance with Gd-DTPA,but the central part will not.thus distinguishing it from epidural scar.[14]

Future Prospectus

In future,it is likely that shift away from CT and myelography and towards MR will continue.New super conductors currently under development will likely operate at higher temperature,perhaps at room temperature and should reduce operating costs.Magnet technology is likely to improve in other ways as well.Gd-DTPA and other contrast will increase contrast between lesions and normal structures in selected circumstances.Further improvement in surface coil technology and fast scan techniques should allow the complete spine to be imaged in a reasonable time frame.Increasingly,this will allow MR to compete favourably with myelography and quite possibly replace it.

Conclusion

MR has rapidly evolved as a primary imaging modality for evaluating the spine.It competes favourably with CT in all areas except in evaluating bone detail and following myelography.It is currently the preferred study in patients with myelopathy,radiculopathy and in many other clinical circumstances.MR of the spine is likely to become an even more important examination as the technology evolves and it may replace myelography entirely for many indications.

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ALUMINIUM PHOSPHIDE POISONING (DIAGNOSIS AND MANAGEMENT)

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Introduction:

Aluminium phosphide (ALP), a solid fumigant pesticide, is used worldwide to store grains. It is available as grey coloured, 3g. tablets with various names like Alphos, Celphos, Quick phos. One tablet liberates 1.0g of phosphine ($PH3$) gas after coming in contact with moisture of grains or hydrochloric acid of stomach which is responsible for toxic effects in humans.

$$ALP + 3HCL3 — ALCL3 + PH3 \quad I$$
$$ALP + 3H_2O — AL(OH)3 + PH3 \quad II$$

It is fast becoming an easy suicidal agent as it is easily available, cheap and extremely lethal with mortality rate varying from 37-100%. Majority of patients die early due to shock, cardiac arrhythmias, ARDS or acidosis.

Mechanism of action of ALP is still not well known. Many believe that there is inhibition of enzyme cytochrome oxidase, (Nakakita 1971 and Chetulka et al 1976), inhibition of catalase and generation of oxygen free radicals (Prince NR et al and Bolter CJ) and Chugh et al (1988) showed high superoxide dismutase activity and low catalase level leading to formation of free radicals resulting in accelerated lipid peroxidation.

Diagnosis:

The diagnosis of ALP poisoning, most of the times is obvious but sometimes elusive.

1. Reliable history and production of container.
2. Decaying fish or garlic odour of the breath.
3. Presence of clinical manifestation.

The signs and symptoms of inhalation and ingestional toxicity are:

(a) Inhalational

Mild inhalation: Irritation of mucous membrane, respiratory difficulty, fatigue, light headedness, dizziness, anorexia, nausea, vomiting.

Moderate inhalation: Ataxia, numbness, paraesthesias, weakness of muscles, tremors, diplopia, muscular paralysis and jaundice.

Severe inhalation: Symptoms and sings of multi organ failure, mortality is very high in this group.

(b) Ingestional

Depending upon the dose and the compound ingested:

Mild: Nausea, vomiting, anxiety, abdominal cramps and occasionally hypotension.

Moderate:

GIT: Nausea, vomiting, dryness of mouth, epigastric tenderness, pain abdomen.

CVS: Hypotension, shock, brady or tachy arrhythmias, pericarditis. ECG may show ischaemic pattern, arrhythmias and conduction defects.

Respiratory System: Difficulty in respiration, basal crepts, type I or type II respiratory failure.

Hepatobiliary: Jaundice, tender hepatomegaly, acute hepatic failure, raised transaminases.

Renal: Oliguric or non oliguric ARF.

CNS: Anxiety, depression, fear and undue crying, convulsions and coma are rare.

Severe: Signs and symptoms of multi organ failure rarely encountered.

Confirmation of phosphine toxicity:

The confirmation of diagnosis is either done by qualitative silver nitrate paper test or detection of $PH3$ in blood (Calorimetric or liquid gas chromatography).

Management:

Early diagnosis and immediate intensive management of ALP is mandatory. There is no specific antidote, treatment is mainly symptomatic and supportive.

(A) To retard absorption of phosphine from G.I. Tract:

1. Gastric lavage with KMNO 4 (1:10000 dil or $MgSO4$) is carried out immediately to oxidize the unabsorbed poison.
2. Activated charcoal 100g orally or through

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nasogastric tube to absorb poison.

3. Antacids and H2 blockers to be used for symptomatic relief.

(B) To Check cellular toxicity of PH3

Cellular toxicity of PH3 is due to oxygen free radicals. Magnesium has been found to be useful in combating this due to its antihypoxic antiarrhythmic and membrane stabilizing properties (Chugh et al 1994). The dose is 1g IV stat, then 1g one hourly for next 3 hours followed by 1g IV every 6 hours till final outcome or upto maximum of 5 days, although higher doses have been used without any significant effect on mortality.

(C) To increase PH3 excretion:

Maintain adequate hydration and renal perfusion with I/V fluids, if ARF develops then dialysis support: haemodialysis, or continuous diafiltration haemodialysis CAVH/CAAH.

(D) Supportive measures:

1. Treatment of Hypoxia and ARDS.
   - ◆ Oxygen administration through ventimask.
   - ◆ Patent air way by endotracheal tube in unconscious patients.
   - ◆ Assisted ventilation whenever required.
   - ◆ If ARDS develops then patients should be managed in respirative I.C.U with mechanical ventilation. Arterial blood gas analysis should be done.

2. Treatment of shock.

3. Treatment of arrhythmias.
   Magnesium an intracellular cation is a potent antiarrhythmic and membrane stabilizing agent has been found effective in reducing the incidence of arhythmias and improving the prognosis.

4. Treatment of metabolic acidosis. In moderate to severe acidosis (HCO3 less than 15mmol/ ltr.)
   Sodabicarb is administered till PH3 is exereted Sodabicarb 50-100m Eq. is given every 8 hourly for 2-3 days, if acidosis persists dialysis may be attempted.

Causes of death:

1. Cardio vascular collapse or irreversible shock.
2. ARDS.
3. Syndrome of multiple organ failure.

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POSTOPERATIVE PAIN RELIEF: A BASIC HUMAN RIGHT

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Postoperative pain is generally inadequately recognised, inadequately monitored and inadequately treated[1]. Recently advances have been made to reduce the incidence of postoperative pain and increase the efficacy of the treatment through the increased awareness of the incidence, severity, and consequences of postsurgical pain. It needs determination of both surgeons and anaesthetists to consider at every stage of the operative process, ways to eliminate pain with the greatest efficacy for the least risk. When the methods of effective analgesia have inherent dangers, efforts are being directed towards the elimination of risk by better supervision, monitoring and treatment of pain after surgery. In postoperative wards improvements have been achieved because of better monitoring of pain, and by greater reluctance of the patients, nurses and medical staff to accept the persistence of severe pain. They have been achieved by forethought in the provision of pre-emptive analgesia, by systemic and regional analgesia, by both surgeon and anaesthetist. The benefits of effective analgesia are weighed against the risk of analgesic therapy, and the risks are reduced to minimum. Analgesia should be more aggressive, time consuming or invasive, when the pain is inevitable and severe. The analgesic drug chosen nowadays is more likely to reflect the type of pain, as much as the severity, and a balanced mixture of analgesic drugs and measures can be used to reduce the side-effects of any one method.

In western countries the establishment of "actue pain team" is perhaps the single most effective measure to deal with this problem. Such team consists of interested and enthusiastic clinicians, who, supervise postoperative analgesia and encourage pre-, post and interoperative ways of reducing and eliminating pain[2,3].

Pathophysiological Consequnces of Postoperative Pain

Postoperative pain differs from other types of pain in that it is usually of short duration with progressive lessening of pain over a period of day or two. This acute pain is more responsive to treatement than chronic pain which is persistent, varies in intensity and is associated with varying degrees of depression. In addition to humanitarian reasons we must relieve postoperative pain because.

1. Pain stops deep inspiration and thus an effective cough to clear secretions.
2. Poor chest expansion leads to retention of secretions, pulmonary collapse and bronchopneumonia.
3. Shallow respiration leads to reduced Functional Residual Capacity (FRC) and makes patient more prone to alveolar collapse hence postoperative hypoxemia[4].
4. Pain leads to reduced movements which predisposes the patient to venous stasis, deep vein thrombosis and pulmonary embolism.
5. Pain increases severity of metabolic response to trauma.
6. Pain increases sympathetic activity, heart rate, blood pressure, periphral resistance and cardiac work.
7. Pain decreases intestinal motility.
8. Pain increases the chances of myocardial ischemia in those with coronary artery disease[5].

The intensity and duration of postoperative pain varies markedly between individuals. The patients response to a pain depends upon the cause, the location, its severity, psychological makeup and pain sensitivity.

Analgesic requirements vary depending upon;

1. Site and type of surgery: Thoracic, upper abdominal surgery and surgery on joints is associated with greater pain than lower abdominal surgery.
2. Age and sex: The requirements for analgesia are the same between males and females for a given surgical operation and the requirements decrease with increasing age.
3. Patients psychological makeup: Anxiety tends to be associated with increasing postoperative pain perception and increased analgesic requirement.
4. Pharmakokinetic variability: Variability in rate of absorption, distribution and metabolism of a drug occurs between patients.
5. Pharmakodynamics variability: Difference in sensitivity of receptors occurs between patients.
6. Discomforts which exacerbate pain perception such as nausea, presence of nasogastric tube and a dry

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mouth.

Methods of Postoperative Pain Relief

- Psychoprophylaxis.
- Pre-emptive analgesia.
- Opiods.
- Local anaesthesia.
- Cyclo-oxygenase inhibitors.
- Volatile anaesthetics.
- Others like Transcutaneous electric stimulation & Cryotherapy.

Psychoprophylaxis

The ability to control pain varies with the type of personality[6], the ability to communicate, the retention of personal identity[7]. Proper preoperative communication with the patient does reduce the postoperative pain and the need for analgesia to a great extent. Patients must be told not only of intraoperative procedure, but what experiences to expect and how to cope with them[8], including how to obtain analgesia. Preoperative visit of anaesthetist has been shown to reduce the anxiety by 11%[9], also a 25% reduction in anxiety and opiod requirement following a 7.5 minute audiovisual presentation of perioperative procedures, the reasons and the methods of pain management and prrvention.

Pre-emptive analgesia

It has been proved by experiments in humans and animals, that pre-emptive treatment of pain, especially by opiods and local anaesthesia, reduce pain for much longer than the expected action of the drug[10]. Nociception causes changes in the central processing of the peripheral nerve and spinal cord, increases the peripheral release of nocigenic neurotransmitter, enlarges the receptive field of nociceptive afferent nerve[11], and induces 'wind-up' of sensitivity at post synaptic spinal cord neurone[12,13]. Pain due to hyperexitable states of cord requires relatively small amount of opiods to prevent but large amounts to relieve[14]. Pre-emptive analgesia can reduce or eliminate the phantom limb pain[15]. The use both local anaesthesia and opiods, pre-emptively, prolongs the analgesic action of both agents[16].

Opiods

Parental opiate therapy is usually not required for more than 48 hours except perhaps in patients who have undergone upper abdominal or thoracic surgery. Opiates can be given via following routes:

a) **Intra muscular route:-** This is the most commonly route used and dose is usually given 4 to 6 hourly. Care is to be taken to avoid ventilatory depression or addiction. There can be variable absorption of drug in hypotension, hypovolumia or hypothermia. If the circulation is poor, the onset of analgesia and peak plasma levels are delayed. Moderate doses are given frequently by injection before acute pain appears, to avoid low plasma levels where there is poor pain relief and high plasma levels where respiratory depression occurs. Care must be taken to watch for overdose in debilitated patients and in very young and elderly. Morphine commences to act in 15-20 minutes, with peak effects at 45-90 minutes. Various opiods used are:

Morphine	10mg.	4 hourly
Papaveratum	20mg.	4 hourly
Pethidine	100mg.	3 hourly
Pentazocine	60mg.	4 hourly
Dihydrocodeine	50mg.	4 hourly
Buprenorphine	0.3 - 0.6mg.	6 hourly.

The effects of opiods can be antagonized by Naloxone 0.1-0.4mg. in case serious side effects like respiratory depression occurs.

b) **Bolus Intravenous Injection:** Small doses of opiods given i.v. e.g. Fentanyl can lead to improvement of pain relief in the postoperative period. The technique is usually only performed by the anaesthetist in the early recovery period. Rapid depression of ventilation can occur and the patient must be closely watched for any signs of respiratory depression and drowsiness.

c) **Cutaneous Intra Venous Infusion:** This technique has been used to produce analgesia in patients on Intermittent Positive Pressure Ventilation in the Intensive Therapy Unit. It has also been used in general surgical wards to produce analgesia in spontaneously breathing postoperative patients. There is great danger of respiratory depression with this technique. Loading dose of 100 mg. Pethidine or 10mg. Morphine over 30 minutes then infusion of pethidine 25 mg./hr. or morphine 2.5mg/hr. is usually effective in an adult.

d) **Patient Controlled Analgesia (PCA):-** In this technique the patient can in part determine the rate of I.V. administration of an analgesic. Patient being the best judge of onset and severity of his pain, and the level of discomfort tolerable to him, self administration of analgesic and restoration of control of pain reduces anxiety and expectation of pain and increases the pain tolerance and threshold. There is feed back control matching analgesic administration to pain level. There are safety features present to limit the preset dose, the number of doses of analgesic which can be administered and the "Lock out" period between doses.

The system consists of a reservoir of drug, a delivery system, a device for measuring a bolus (a pump, a roller or a small capacity cuvette), a trigger, a clock for setting an interval between one bolus and another, and sometimes, the means of a continuous is required if the patient is to feel in control of the pain. the patient is taught to make a demand for analgesia by pressing a button when pain is experienced; a bolus is delivered, but any other demands during the following lock out interval will not be met by deliver of further boluses. The number of demands can be reduced by the incorporation of a simultaneous continuous infusion of a drug. However, the number of demands is not reduced proportionately, and the amount of opiod consumed and the incidence of ventilatory depression are increased in presence of a background infusion. Although most of the opiod analgesics can be used by this methods, the most usual regimen is for 1 mg. Morphine to be used as the bolus, with a lock-out interval of 5 minutes, with little or no background infusion. Owen et al[17] found that, with a lock-out interval of 5 minutes, a 2 mg bolus caused ventilatory depression in 20% of patients and a 0.5 mg bolus failed to achieve pain control in 30%. The commonest reservoirs are 30 or 60 ml and a concentration of 1 mg/ml of morphine is standard, although a higher concentration is required if most postoperative periods are to be covered by one reservoir.

e) **Sublingual route:-** Some lipid drugs like Buprenorphine are very effective by sublingual route. The drug if swallowed is mostly inactivated. It provides reasonable analgesia following abdominal surgery and also produces marked sedation.

f) **Rectal route via suppository:** This route can be used to deliver morphine, but plasma concentrations are very variable. Venous blood from lower rectum passes to systemic circulation and from upper rectum to portal circulation. So the site of suppository in rectum is very important.

g) **Transdermal route:** Fentanyl has very high lipid solubility and can readily be absorbed through to provide effective plasma concentration.

h) **Spinal and extradural opiates:** Spinal-When opiate is injected into CSF, it is taken up by substantia gelatinosa region of the spinal cord, and is also taken from CSF into circulation. It produces powerful postoperative analgesia without the risk of sudden hypotension. The spinal application of opiods has been reviewed at stages in its development[18,19,20,21]. However soon after the inception of the method, it was discovered that epidural or intrathecal opiods could lead to profound and sudden respiratory depression, even after an interval of several hours after administeration. This is specially true of morphine because of its relative lipid insolubility, but also occurs with lipid soluble opiods as fentayl.

Extradural: when opiate is injected into extradural space, the drug diffuses through dura into the CSF and produces analgesia by the same mechanism as when the subarachnoid space is used. There is rapid uptake of opiate into the circulation from blood vessels in the extradural space. The rate of distribution is determined by lipid solubility and dissociation constants. Intradural, morphine, which is relatively lipid insoluble, is distributed predominent in the CSF rather than to the cord. Here it can act as depot of analgesia and the duration of action of epidural or subarachnoid morphine is longer than that of any other common opiod given by these routes. Drugs in CSF are subject to diffusion and mass movement, especially on straining or change of position. The mobile drug may reach the brain slowly by diffusion, or suddenly by mass movement, and cause itching, somnolence and depression of breathing. Opiods depress ventilation by reduction of sensitivity to carbon dioxide, the reduction of hypoxic drive and by causing disorder in rhythmicity of the ventilatory pattern. Diamorphine is intermediate in its properties and may have the advantages of both. It is two hundred times more lipid soluble than morphine (although much less than fentanyl) and it is less dissociated at body temperature so that it is absorbed more completely more rapidly into the spinal cord than morphine[22]. The intermediate metabolite of diamorphine -6-acetyl morphine also crosses membranes more readily than would be expected from its polar properties[23]. Its duration of action is not as long as that of morphine[24], but it is metabolized to morphine within the spinal cord[25], distributed to the non-lipid sites and is subject to the same delay in release from neural tissue as is morphine. It may therefore be ideal opiod for intraspinal use.

Local Anesthetics

Excellent pain relief can be achieved in the early hours of postoperative period by the use of local anesthetics Various ways of using this technique are:

a) **Wound infiltration:** At the end of the procedure wounds are infiltrated with local anaesthetic like bupivacaine and postoperative pain relief upto 4 hours can be easily achieved. Laparotomy wounds are infiltrated before skin closure, close to the lateral end of rectus sheath on either side where the cutaneous nerves enter into it.

b) **Spinal Nerve Block:** Spinal anaesthesia is produced by injecting local anaesthetic into subarachnoid space through a lumber puncture needle inserted between 3rd and 4th lumber vertebra. Subarachnoid analgesia is not long lasting (less than 4 hours).

c) **Extradural Block:** This can be achieved by using an extradural catheter which is inserted into the epidural space and a bolus of 10-15 ml of 5% bupivacaine is injected through it followed by an infusion of 15-20 ml per hour of 0.125% bupivacaine. This produces very good analgesia after lower abdominal surgery. For thoracic surgery the extradural catheter is inserted between thoracic 7 and 10 vertebrae. An initial dose of 4-6 ml of 0.5% bupivacaine, followed by 6-10 ml per hour of 0.125% bupivacaine, enables the patient to cough, take deep breaths and coperate with physiotherapy. Care is to be taken as hypotension and total spinal block can occur. Spinal and epidural analgesia block sympathetic outflow leading to arteriolar dilatation and hypotension.

d) **Caudal Block:** This can be in patients undergoing circumcision, anal and perianal surgery. Anaesthesia of sacral root is produced by injecting 0.5% bupivacaine via a needle inserted through the sacral canal into the epidural space. It is important to give a test dose first.

e) **Intercostal Block:** This route is used to produce pain relief after thoracic and abdominal surgery and also allows physiotherapy to be instituted. Pain relief can also be achieved in patients of rib fractures in this way. A dose of 3 ml of 0.25% bupivacaine is injected adjacent to each nerve. Bilateral nerve block is not performed because of the risk of pneumothorax.

f) **Paravertebral Block:** After thoracic and abdominal operations local anaesthetic can be injected into the paravertebral space to block the dorsal roots near the vertebral foramina and good pain relief obtained.

g) **Femoral Nerve Block:** It is used for pain relief after arthroscopy of knee joint.

h) **Intrapleural Analgesia:** This method was first described in 1984[26] and has been used to relieve postoperative, post traumatic and persistent pain, in both adults and children. Intrapleural cannulas can be inserted percutaneously, either by loss of resistance or the hanging drop techniques[27] and 8-30 ml of 0.25% 0.75% of bupivacaine are used[28]. The higher concentration gives a longer duration action and the higher volumes give wider spread of nerve blockade. Even after 20ml of 0.75% bupivacaine, the maximal plasma concentration is 1.2mcg/ml, at which toxic effects are unlikely[29]. The addition of adrenaline to the injectate reduces the maximal plasma concentration of bupivacaine. This technique has proved to better than intercostal nerve block in unilateral incisions[30].

i) **Intra Abdominal Analgesia:** Recently intra-abdominal analgesia with 80ml 0.125% bupivacaine has been shown to be effective in the prevention of shoulder tip pain after laproscopic cholecystectomy.

Cyclo-Oxygenase Inhibitors

These drugs are variously referred to as cyclo-oxygenase inhibitors, the prostaglandin inhibitors, the endoperoxidase inhibitors, or the non-steroidal antiinflammatory drugs (NSAID). Paracetamol inhibits brain cyclo-oxygenase in vitro, but it has little or any anti inflammatory activity. The published use of non-steroidal anti-inflammatory drugs for postoperative pain has been recently and thoroughly reviewed[31], but the place for individual drugs, and the drugs as a group, has yet to be established. For dental and minor orthopedic pain, NSAID are at least as effective as low doses of opiods. For moderate to severe pain, NSAID may eliminate the need for opiods in some, and reduce the need for opiods in most patients. Various other agents of this group include.

Asprin, Codiene, Ibuprofen, Naproxen and Diclofenace. NSAIDs are especiallly very useful for day-case surgery since they have minimal effects on sensorium, the gut, bladder or vomiting centre.

Volatile Anaesthetics

Volatile Anaesthetics like Entonox (50% oxygen, 50% nitrous oxide) can be used for pain relief at accidents in the field or for changing burn dressing. Bone marrow depression can occur with prolonged use.

Other Methods

a) **Transcutaneous Electrical Stimulation:** This technique is used to relieve mild to moderate type of pain. A low voltage (0.2-20 Ohz) alternating current is passed between two electrodes on the skin. Large diameter nerve fibers are stimulated and concentration of endogenous opiates are increased in the Central nervous system.

b) **Cryotherapy:** In this method the intercostal nerves are exposed to subzero temperatures on the end of a probe, the nerves are exposed to subzero temperatures on the end of a probe, the nerves are temporarily damaged leading to cessation of nerve conduction for some months. However when sensation returns there may be parasthesia and neuralgia which can be unpleasant.

In summary one must realize the fact that it is the basic right of every patient to be pain free after a surgical procedure is performed on him. The main idea of development of anaesthesia was to render a patient pain free during a surgical procedure, as used to happen in pre-anaesthetic era. Also we must realize that the painful. state of the patient does not end at the end of a surgical procedure when the anaesthesia is switched off, but patient continues to have a fresh surgical wound on his skin, and a huge area of dissection underneath it, which could give him lot of discomfort and pain in the early postoperative period. In addition to humanitarian reasons, the postoperative pain must be relieved as it can lead to significant morbidity as discussed above in pathophysiology. Postoperative pain being a preventable and treatable cause of morbidity, it should be treated enthusiastically and aggressively, minimizing the risk of pain relief by improved monitoring and supervision. A multidisciplinary approach with the formation of "Acute Pain Team" with the established guidelines for analgesia within a postoperative high dependency unit, can only be a real way to give a suffering patient his basic right.

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TRAUMA VICTIMS IN PSYCHIATRY PRACTICE — NEED TO REVIEW CURRENT NOSOLOGY

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Abstract: *Building up on our observations in clinical practice of psychiatry in Kashmir, a systematic evaluation of patients who had experienced a traumatic event of the nature and severity to fulfill the criterion A of Post-traumatic Stress Disorder, was carried out to determine whether it generates one or several psychiatric diagnosis. Results showed that trauma victims in clinical setting qualify for a variety of diagnostic entities.*

Conclusion: No single diagnosis adequately covers the manifestations that result from experiencing trauma. A review of current nosology is recommended, and introduction of an umbrella diagnosis that would encompass symptoms from various diagnoses in to a single symdromic entity - Posttraumatic syndrome.

Key Words: *Trauma, Posttraumatic Stress disorder (PTSD).*

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Introduction

Kashmir has been in the grip of violence for over a decade. The situation prevailing here has at times been referred to as"low-intensity war," and represents the worst period in the history of the valley in terms of bloodshed and loss of life and property. In terms of loss of life alone, scores got killed with such a regularity that unusual would be a day that would end without such an occurrence. On one hand, armed conflicts erupt every now and then at different places resulting in damage to life and property, on the other hand various events keep recurring e.g. crackdowns (Search Operations), arrests, torture, kidnappings, armed robberies etc. Still more, unidentified dead bodies are fished out from rivers, streams and gutters, and also people are reported to be missing. The types of events occurring here are, like all others, reported in literature on traumatic stress, a replication of man-to-man brutalities found elsewhere on the globe.

Under the circumstances described, traumatic stress remains a major accompaniment of life of people living in Kashmir. The various types of traumatic events occurring have all the characteristics that have been implicated in the etiology of various trauma related psychiatric disorders. Although, modern psychiatry provides the much required observational frame work for studying the effects of trauma under the diagnosis of posttraumatic stress disorders (PTSD), in clinical practice of psychiatry in Kashmir trauma victims qualify for an array of diagnoses, thereby prompting one to rethink over the status of trauma victims. The ideal way to address this issue would be a community-based research because of the possibility that given the frequent occurrence of trauma in the valley, the majority of the victims may not come in contact with specialized medical services. However, a community research in the prevalent circumstances remains a remote possibility owing to the security risk involved in such an endeavor and lack of funding agencies. Therefore, a systematic evaluation of trauma victims was done in a private psychiatric clinic. A report of the same in presented here.

The goal of the present study was to know the psychiatric status of trauma victims in a clinical setting, whether experiencing the type of events as mentioned under criterion 'A' of PSTD in DMS-III R resulted in a clinical diagnosis of other disorders also.

Material and Methods:

Keeping in view the observation[1] that trauma survivors may present to non-psychiatric physicians for treatment of somatic problems, referrals were sought from some non-psychiatric physicians in the town. These, along with those who volunteered from treatment in a private psychiatric clinic were routinely assessed for inclusion in the study. The inclusion criteria was the occurrence of a traumatic event that had the generic characteristic of the events mentioned under the criterion 'A' of the PTSD in DSM-III R[2]. The psychiatric evaluation was done using SCID[3] that helps generate DSM-III R diagnoses. Screening for the presence of trauma was done using list of Threatening experiences, interview version (LTE-I)[4].

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This comprises of questions regarding twelve negative events of common occurrence. Probing was done regarding the circumstances surrounding the occurrence of the events if any, so as to fulfill the criterion 'A' of PTSD in DSM-III R. In the event that the patient's response to LTE-I was negative, same was administered to a close associate from family or kinship circle, asking about the occurrence of the events to the patient. This was done to minimize the bias of not reporting a traumatic event, which the survivors of such events are known to avoid in order not to get the memories of the original trauma.

Results

Total of eighty five patients met the criterion A of PSTD as per DSM-III R. the mean age of the sample was 35.5 years with a range from 17 years to 60 years. Females constituted 60% of the sample (n=51). Of the various diagnoses major depression constituted 35.3% (n=30) and was the largest diagnostic group. Other diagnoses in the descending order were dissociative disorder (20.0%), somatoform disorder (17.6%), PSTD (10.6%), Other Anxiety disorders (12.9%), and other diagnoses (3.6%).

The results show that people who have met traumatic events of the nature and severity that could qualify them for the development of a specific disorder, may in clinical setting develop various other disorders and hence there presentation also is varied. The patients receiving PSTD and somatoform disorders as diagnosis, have all initially presented to physicians (non-psychiatric), while as those receiving the diagnosis of major Depression, Dissociative Disorders and others have made initial contact with psychiatrists.

Discussion:

Our study highlights that in clinical practice of psychiatry, truma victims qualify for a variety of diagnoses, and that no single diagnostic entity in the current nosology uniformly addresses this issue. Although PTSD has emerged as a major focus of traumatic stress research in recent years, other diagnoses viz Major Depression, Dissociative disorders and Somatoform disorder remain equally significant and should receive renewed attention in Psychiatric research. Numerous studies since world war II have demonstrated high prevelence of chronic Depression, Anxiety and Somatization in persons exposed to traumatic events[5-10]. Depression and Somatization along with PTSD have been reported in Southeast Asian refugees[11] who had to witness worst kinds of traumatic events in modern civilized era. There is abundance of research linking Dissociation with trauma. Freud[12], Jenet[13] and William James[14], the pioneers of Psychiatry, all have reflected upon this relationship.

Interestingly, PTSD, Dissociative Disorders and Somatoform disorder are psychodynamically linked through the mechanism of dissociation. In DSM-IV, Dissociative symptoms are included in the criteria for acute stress disorder, PTSD, Somatization disorder, and Dissociative disorders themselves. Modern Psychiatry in rediscovering the intimate relations among trauma, Dissociation, Somatization, and a host of psychological problems[1]. Many studies have demonstrated a strong relation between trauma and Dissociative symptoms.

In view of the above, it may be stated that, to adequately cover the clinical manifestations in trauma victims we need to have an umbrella diagnosis that is based on the psychodynamics of Dissociation and encompasses symptoms from such related disorders as PTSD, Dissociation and Somatization disorders. For this, a more appropriate term could be "Postraumatic Syndrome". It may be noted that the major impetus behind the research on PTSD has been the perceptible need of how to address the psychological status of trauma victims. The studies addressing this issue have been conducted mostly in the community samples, rather than on patient sample. At present, the state of affairs is such that PTSD has been recognized even in women who have suffered trauma, especially, trauma early in life[15], and who continue to remain within the functional normality if not asked about the occurrence of such events and the consequent aberrations of psychological functioning. But the patient population remains a different class, in the sense, that they voluntarily come out seeking treatment for something that they perceive as abnormal. Therefore, equating a traumatized adult male with an apparently normal women who has memories of early trauma in childhood, almost belittles the status of our patient population. Hence, the need for reviewing the status of trauma victims.

Conflict of Interest: None

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OBSERVATIONS ON LONGTERM RESULTS OF METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS IN KASHMIR

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Abstract: *This open, controlled and non-comparative study was conducted on 101 patients of Rh. arthritis fulfilling ACR criteria to observe the long term efficacy and side effects of low dose methotrexate with a followup period of 24-36 months. Patients with a mean age of 46±4 years and a male to female ratio of 1 : 3.4 were assessed on clinical and biological parameters. Fresh as well as old cases who had taken other DMARD's and steroids were also included. NSAID's and steroids were tapered off gradually in all patients. Clinical improvement occurred within 6-8 weeks in 79 patients and in remaining 22 patients remission was achieved upto 24 weeks. All the six parameters showed significant improvement with Mtx therapy. Pain and morning stiffness decreased significantly from a base line mean values of 6.56±1.28 and 76.62±9.68 to 0.48±0.86 and 3.28±6.21, respectively. Articular Index changed from 16.62±4.53 to 0.386±0.562 and grip strength from 23.80±8.61 to 127.7±42.58 at 36 months followup. Laboratory values such as haemoglobin and ESR also showed significant improvement from a base line mean values of 10.7±1.75 to 12.6±1.26 and from 33.1±15.63 to 7.81±6.18 respectively. The side effects observed were very mild (24%), amenable to folic acid therapy and antacids. Few patients developed transient bone marrow depression and elevation of liver enzymes, not needing withdrawal of drug. In 5% patients the drug had to be withdrawn because of repeated skin rashes. Hence we conclude that Mtx is a reliable drug for long term benefits in patients with a life long disease such as Rh. arthritis because it has significant efficacy-to-toxicity ratio as compared to other drugs.*

Key words: *Methotrexate, Rheumatoid Arthritis, Efficacy, Side effects.*

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Introduction

Rheumatoid arthritis is a chronic, progressive, multisystem inflammatory disorder of middle aged adults with a prevalence rate of 1% approximately[25]. The inflammatory process of proliferating synovial membrane is immune-mediated leading to destructive articular changes[4]. It is a systemic arthritis involving numerous small and large joints with repeated attacks of synovial inflammation causing articular cartilage damage with bony erosions, leading to a substantial risk for mobidity, disability and even mortality.

Sero-positive rheumatoid arthritis is more aggressive and can make a patient crippled with deformities in a short course of time[9,27]. Hence modern thinking revolves around early aggressive attack of disease by disease-modifying drugs which stop progression of disease, thereby reducing joint pain and swelling; this allows early physiotherapy and exercises for maintaining joint function and joint protective measures can be applied for prevention of joint deformities[19,23,26,27].

The primary goal of therapy is to relive pain, preserve function, reduce inflammation, protect articular and extra-articular structures, control disease-progression and its systemic complications and avoid adverse drug reactions[13,14]. This is achieved by the patient education, physical therapy, vocational counselling, non-drug therapies (heat and cold, ambulatory assistance devices, splinting) pharmacological agents (oral, parentral and topical) and surgery. Hence the treatment of the disease is multidisplinary.

Methotrexate is quickly acting disease-modifying agent and halts the progression of bony erosions, thereby preventing joint deformity and morbidity. It is cheap with good compliance having weekly convenient dosage and has minimal side-effect[9,10,22,27]. Mtx (N-10 methyl-aminopterin) is a folate analogue and an ideal drug for rheumatoid arthritis being used on large scale worldwide. It is given at a very low dose with more rapid onset of action (2-6 weeks) than other DMARD's. It fulfills most of the qualities of an ideal drug[19,22,26,27].

Material and Methods.

This study was conducted on 101 patients of either sex and between the age range of 18-70 yrs, in the

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department of Physical Medicine and Rehabilitation, SK Institute of Medical Sciences, Srinagar (J&K) from 1996 to 1999. Patients of Rh. arthritis fulfilling the ACR criteria were given Mtx on long term basis to assess the efficacy, tolerability, compliance and side effect profile of the drug. The study was of an open, controlled and noncomparative design and the period of trial was 24-36 months. All the patients were allowed to continue their usual non-steroidal anti-inflammatory drugs (NSAID's) and those who were on steroids were allowed to continue, with the dose being gradually tapered off.

All the patients after informed consent were given 7.5 mg of MTx per week, in an intermittent pulse regimen[22,27]. Baseline investigations such as haemogram, urine, KFT, LFT, Rh. factor, CRP, ASO, ANA and immunoglobulins, X-ray chest and X-ray both hands AP view were done in all cases[9,18,26,27]. MTx dose was increased gradually to a maximum of 20mgs/week in patients with insufficient response[27].

The admission criteria were fresh as well as old cases with failure to continue other DMARD for a minimum period of 3 months due to non-effectiveness, non-availability, cost factor or side effects[22,23,27]. Patients with skin rashes, haematological, renal or hepatic disorders, uncontrolled diabetics, malignancy, pregnant women, blood dyscrasias and very old patients were excluded from the study[16,22,27].

MTx was stopped if pulmonary, haematological side effects developed or when transaminase levels rose above twice the upper normal limits. MTx was reintroduced when the tests returned to normal. For other side effects (gastrointestinal, transaminase below twice the upper limit of normal and alopecia), folic acid was given 5mg daily which was increased upto 10mgs/day, when side effects were not controlled effectively.

Assessment and follow-up

The follow up of these patients was carried out at 4 wks, 3 months, 6 months, and 6-monthly thereafter upto 24-36 months. Laboratory investigations such as CBC, LFT, KFT, Lung Function Tests were done to monitor the toxicity of MTx. The clinical assessment of disease activity was made according to the index developed by Mallya and Mace[28]. This index includes six parameters viz:-

- two subjective (morning stiffness and pain scale)
- two semisubjective (grip strength and articular index) and
- two objective (haemoglobin and erythrocyte sedimentation rate (ESR).

Each of the above six parameters were divided into four arbitrary grades as shown in table I.

Table I: Grading of clinical activity

Grade	MS	Pain S	GS	AI	Hb%	ESR
I	<10	0-2.4	>200	0	>14.1	0-20
II	10-30	2.5-4.4	50-200	1-7	13-14	21-45
III	31-120	4.5-6.4	21-49	8-17	10-12.9	46-80
IV	>120	6.5-10	<20	>18	<9.9	>81

M.S= Morning stiffness in mts.; PS = Pain(score); G.S = Grip strength; A.I = Articular index; Hb% = Haemoblogin; ESR = Erythrocyte sedimentation rate.

Each of these parameters were measured as described under:

1. Hb: It was measured at each sitting by cynmeth haemoglobin method.
2. ESR: It was measured at each sitting by Wintrobe's method
3. Duration of morning stiffness: It was measured in minutes.
4. Pain: This was represented by a ten centimeter horizontal line drawn on outpatient card which was graduated from 0-10, marked with 'no pain' at one end (marked 0) and 'worst possible pain' at the other end (marked 10). Patient would represent the severity of pain by putting a cross mark on relevant centimeter mark.
5. Grip strength: This was measured at each sitting by using an ordinary sphygmomanometer.
6. Ritche's Articular Index: At each sitting fifteen groups of joints were studied and tenderness was elicited by firm pressure or passive movement and were graded as under:-

GO - Patient had no tenderness
GI - Patient complained of pain
GII - Patient complained of pain and winced
GIII - Patient complained of pain, winced and withdrew.

Sum of the total grades was calculated from all joint groups. These parameters were assessed at start of trial and at 4 weeks, 3 months, 6 months, 12 months, 18 months, 24 months, 30th and 36 months[24].

Table II: Age & Sex distribution

Total No. of patients	Male	Female	M : F ratio
101	23	78	1 : 3.4

Age ranged from 18-70 yrs with a mean age of 46±4 yrs

Remission Criteria

Patients were considered in clinical remission when they fulfilled at least minimum of five following requirements for at least 2 consecutive months.

1. Morning stiffness of no > 15 minutes.
2. No fatigue
3. No joint pain

4. No joint tenderness or pain on motion
5. No soft tissue swelling in joints or tendon sheatns
6. ESR of < 30 mm/hr.

Table III: Pain score (Ranged from 0-10, classified into four grades as follows)

No. of patients: 101

Pain score	Baseline	4wks	12wks	6mths	12mths	18mths	24mths	36mths
Grade I (Score 0 - 2.4)	-	-	95	95	96	96	96	99
Grade II (Score 2.5 - 4.4)	-	83	4	6	5	5	5	-
Grade III (Score 4.5-6.4)	47	18	2	-	-	-	-	-
Grade IV (Score 6.5-10)	54		-	-	-	-	-	2

OBSRVATIONS AND RESULTS

This study was conducted on 101 patients of rheumatoid arthritis with a male to female ratio of 1:3.4. The age of these patients ranged from 18 yrs-70 yrs with a mean age of 46±4 yrs(Table II).

The duration of the disease ranged from 3 months to 10 years. 36 patients had taken other DMARD's previously and 18 patients were on steroids. 90 patients were rheumatoid factor (+ve) and 11 patients Rh. factor negative. All clinical and biological parameters assessed; improved significantly as shown in tables. Most of the patients showed improvement at 4 weeks follow up. Patients who were on corticosteroids and NSAID's were tapered off within 6-12 weeks. The improvement in various parameters was as follows:

Table IV: Morning stiffness: (in minutes, graded in 4 groups)

No. of patients:101

Morning stiffness	Baseline	4wks	12wks	6mths	12mths	18mths	24mths	36mths
Grade I (>10 mts)	-	-	99	99	99	99	98	98
Grade II (10-30mts)	-	70	02	02	02	02	3	01
Grade III (31-120 mths)	97	31	-	-	-	-	-	-
Grade IV (>120 mths)	4	-	-	-	-	-	-	2

Table V: Articular Index

No. of patients = 101

Articular Index (grades)	Baseline	4 wks	12wks	6mths	12mths	18mths	24mths	36mths
Grade I (A 1=0)	-	-	12	90	98	98	99	99
Grade II (AI 1-7)	-	4	85	10	3	3	2	-
Grade III AI 7-17)	71	35	2	1	0	0	0	-
Grade IV (AI of > 18)	30	26	2	0	0	0	0	2

Pain: At the onset of study 47 patients had grade 3 score and 54 patients had grade 4 score. At 4 weeks 83 patients had grade 2 score and 18 patients had grade 3 score. Pain score progressively improved in all patients and at the end of 18 months 96 patients had score of grade I and 5 patients had score of grade II. By 24-36 months all patients had score of grade I except 2 patients who had score of grade IV due to disease recurrence(Table III).

Morning stiffness: At the onset, 97 patients had grade III and 4 patients had grade IV morning stiffness. At 4 weeks 70 patients had grade II and 31 patients grade III morning stiffness. Morning stiffness progressively improved in all patients and at the end of 24 months 98 patients had grade I and 3 patients had grade II morning stiffness. By the end of 36 months 98 patients had grade I, one patient had grade II and 2 patients had grade IV morning stiffness (Table IV).

Articular index: At the onset of study 71 patients had grade III and 30 patients grade IV articular index. At 4 weeks 40 patients had grade II, 35 patients had grade III and 26 patients had grade IV articular index. At 12 weeks, 12 patients had grade I and 85 patients had grade II articular index. At 18 months 98 patients had grade I and 3 patients had grade II articular index. At 36 months 99 patients had grade I and 2 patients grade IV articular index (Table V).

Table VI: Grip Strength

Grip strength (In grades)	Baseline	4wks	12wks	6mths	12mths	18mths	24mths	36mths
Grade I (GS > 200mmHg)	0	0	0	0	1	53	55	50
Grade II (GS 50-200mmHg)	0	14	91	92	94	44	46	49
Grade III (GS 21-49mmHg)	54	87	10	9	6	4	-	-
Grade IV (GS < 20mmHg)	47	0	0	0	-	-	-	2

Table VII: Haemoglobin

No. of patients=101

Hb. conc.	Baseline	4wks	12wks	6mths	12mths	18mths	24mths	36mths
Grade I (>14.1g%)	3	12	12	30	36	36	36	36
Grade II (Hb 13-14g%)	11	46	78	68	62	64	65	63
Grade III (Hb 10-12.9g%)	57	32	7	0	2	1	0	-
Grade IV (Hb<9.9g%)	30	11	4	3	1	0	0	2

Grip strength: At the onset 54 patients had grade III and 47 patients had grade IV grip strength. At 4 weeks, 87 patients had grade III and 14 patients grade II grip strength. At 12 weeks 91 patients had grade II grip strength. Grip strength progressively improved in all patients and at 24 months 55 patients had grade I, 46 patients had grade II grip strength; at 36 months 55 ha grade I, 49 grade II and 2 patients had grade IV strength (Table VI).

Table VIII: ESR

No. of patients=101

ESR Grading	Baseline	4wks	12wks	6mths	12mths	18mths	24mths	36mths
Grade I (ESR 0 - 20mm/1hr)	25	34	45	50	63	82	90	80
Grade II (ESR 21-45mm/1hr)	53	63	55	50	37	18	18	18
Grade III (ESR 46-80mm/1hr)	23	4	1	1	1	1	3	3
Grade IV (ESR/81mm/1hr)	-	-	-	-	-	-	-	-

Haemoglobin: At the start 57 patients had grade III, 30 patients grade IV, 11 patients grade II and 3 patients grade I haemoglobin concentration. At 4 weeks 12 patients had grade I, 78 patients had grade II, 7 patients grade III and 4 patients grade IV. There was progressive increase in haemoglobin concentration and at the end of 24 months 36 patients had grade I and 65 patients grade II haemoglobin concentration. At 36 months 36 patients had grade I, 63 patients grade II and 2 patients grade IV Hb levels (Table VII).

ESR: At the onset of study 25 patients had grade I, 53 patients grade II and 23 patients grade III ESR. By the end of 4 weeks 34 patients had grade I, 63 patients grade II and 4 patients grade III ESR. ESR decreased progressively and at 12 months, 63 had grade I, 37 had grade II and one patient had grade III. Between 24 and 36 months 80 patients had grade I, 18 patients had grade II and 3 patients grade III(Table VIII).

Table IX: Side effects

Nature	No. of patients		%age
- Nausea, epigastric discomfort	21	GIT	24%
- Vomiting	3		
- Oral ulcers	1		1%
- Fixed drug eruptions	3		3%
- Skin rash (Maculo papular)	2		2%
- Pancytopenia - Bicytopenia	2		2%
- Deranged liver enzymes	2		2%

Table X: Final analysis of clinical and biological parameters with mean values of 101 patients at the end of 36 months follow up.

Parameters	Baseline mean values (±SD)	Final mean values (±SD)
Pain score	6.56±1.28	0.48±0.86
Morning stiffness	76.62±9.67	3.28±6.21
Articular Index	16.62±4.53	0.386±0.562
Grip strength	23.80±8.61	127.7±42.58
Haemoglobin	10.7±1.75	12.6±1.26
ESR	33.1±15.63	7.81±6.68

Side effects

The tolerability of MTx was excellent in this series with minimal side effects in few cases only. The gastrointestinal side effects in the form of nausea, epigastric discomfort and vomiting (24%) were very mild and responded well to folic acid derivatives, H2 blockers and antacids[7,8]. The liver enzymes rose twice above the normal values in two patients[2,21]. Bone marrow depression developed in two patients and it was transient. 3 patients developed recurrent skin rash and the drug had to be discontinued in these patients[26,27]. One patient developed oral ulcers which were treated(Table IX).

Table XI: Longterm results of MTx in various studies

Clinical parameters	Kremer and Philips	K. Acuthan	C. Bolgna	Present study
	1992	1993	1997	1999
No. of patients	29	128	453	101
Duration of followup	84 mths	24mths	35.2±27.9mths	24 - 36 mths
Onset of action	4-6 weeks	4-8 weeks	3-6 weeks	8-12 weeks
Clinical improvement at the end of study	50% - 92%	83%	60%	>90%
Side effects		22%(mild) 7%(severe)	59%(mild)	26%(mild)

DISCUSSION

The primary goal of this study was to observe the long term benefits and side effects of MTx in our patients, who are socioeconomically poor and illiterate with various wrong conceptions about the disease and drugs. 101 patients of Rh. arthritis were given low dose weekly MTx from 24-36 months and they were monitored on biological and clinical parameters. The role of MTx as DMARD of choice, having efficient tolerability, quick and sustained action with low cost factor and good compliance has been established in our set up. Our patients were in the mean age group of 46±4 yrs with male to female ratio of 1 : 3.4. All our patients showed progressive improvement in all parameters within 6-8 weeks except in 22 patients where remission was achieved after 24 weeks of MTx treatment. K. Achuthen et al(1993) had 128 patients with mean age of 28.02±8.6 and male to female ratio of 4:7. C. Bolonga et al 1997) studied 453 patients for long term results of MTx and found clinical improvement significantly after 6 months.

36 patients in our study had taken other DMARD's previously and they showed marked improvement with MTx in 8-12 wks of treatment. Acuthen et al (1993) had 52 patients on other DMARD's in his series. 18 patients who were on steroids improved significantly and steroids were withdrawn within 4-8 weeks, The toxic effects of steroids such as Cushing's syndrome also disappeared.

NSAIDS coadministered initially were withdrawn in 90 patients within 8-12 weeks and the remaining 11 patients, they were stopped within 6 months.

Pain score in our study showed marked improvement from a mean of 6.56±1.28 at the start of therapy to 0.48±0.86 after 36 months. Kremer and Philips (1992)[11] studied 29 patients for 84 months with 50% improvement in pain index. K. Acuthan (1993)[22] showed improvement in pain in 83% patients over 24 months followup.

Morning stiffness improved from 76.62±9.67 to 3.28±6.21 at final followup. K. Acuthen has also seen improvement in M.S from 270 to 132 mts at 24 months. Articular index also improved from 16.62±4.53 to 0.386±0.562 in 36 months of MTx therapy in our series. C. Bolonga (1997)[27] studied 453 patients for 35.2±27.9 months and found improvement from 13.4±9 to 6.6±7 in articular index. K. Acuthen (1993) found significant improvement in A.I in 2 years follow up. Kremer and Philips (1992) found 92% improvement on 84 months follow up in 29 patients in articular index.

In our study grip strength showed improvement from 23.80±8.61 to 127.7±42.58 mmHg after 36 months.

K. Acuthan (1993) found improvement from 228 to 296 in grip strength after 2 years followup. Haemoglobin and ESR also showed marked changes from 10.7±1.75 to 12.6±1.26 and 33.1±15.63 to 7.81±6.68 respectively. ESR changed from 46.5±30.1 to 30.9±23.2 and Hb% from 11.9±1.7 to 12.5±1.6 in the series of C. Bolgna (1997[27].

Side effects in the present series of 101 patients were very mild with 24% patients having G.I.T. symptoms such as nausea, upper abdominal discomfort and vomiting. Other side effects such as cytopaenia were seen in 2 patient which was transient and no withdrawal of MTx was required. Skin rashes developed in 3 patients with every dose of MTx leading to withdrawal of drug. Other side effects were not seen in this series. K. Acuthan 91993) noticed mild side effects in 22% patients and in 7% patients the drug was withdrawn because of other toxic effects. C. Bolgna (1997) found adverse reactions in 59% patients which were mild in nature and amenable to folic acid supplementation.

Conclusion

Methotrexate after being approved by FDA in 1988 has revolutionized and revitalized the treatment of rheumatoid arthritis because of its efficacy, tolerability and sustained action.

In our observational open, controlled and non-comparative type of study on 101 patients of Rheumatoid arthritis on long term followup from 2-3 years with methotrexate at a weekly dose of 7.5 - 20 mg, all clinical and biological parameters showed very good improvement in all patients except 2 patients who had recurrence. Maximum clinical improvement occurred within a mean period of 6-8 weeks in a large number of patients, except in few patients taking 8-12 weeks. Methotrexate has been found superior to all other DMARD's and has steroid sparing effect. Remission as per ACR criteria has not been achieved but overall improvement with active physiotherapy, physical modalities and joint protective measures led to restoration of very good functional capacity of joints with minimal muscle mass atrophy and osteoporosis. Maximum number of patients could resume their daily routine activities and job. In fresh cases the joint integrity has been preserved without any disability or deformity.

Hence we recommend MTx. in all cases of rheumatoid arthritis at any stage of active disease to give maximum benefit of the drug which has a sustained and long term benefits (3-10 years) in patients having a life long disease viz., rheumatoid arthritis. The drug has significant efficacy-to-toxicity ratio as compared to other DMARD's.

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FIRE ARM INJURIES - MANAGEMENT OF TYPE III OPEN FRACTURES OF LONG BONES

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Abstract: *In a prospective study 30 patients with Type III (Gustilo et al) fractures due to fire-arm injuries were treated by external skeletal fixation and followed till union or amputation. 8 patients belonged to Type III a and another 22 patients had Type III b fractures. There were 3 non-unions in Type III a and 12 in Type III b fractures. Secondary amputation was done in Type IIIb injuries[4]. All non-unions were bone grafted after obtaining soft tissue cover with plastic surgical procedures. All non-unions united except one which required centralization of the ulna.*

Key words: *Fire arm Injuries; Fractures.*

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Introduction:

Open fractures are surgical emergencies. The incidence of complications like disability and death after open fractures of bones are challenging problems for the general orthopaedic surgeon. Many different methods of management of open long bone factures due to fire-arm injuries have been advocated but most of these methods have high complication rates like infection, non-union and increased hospital stay. External skeletal fixation, however, has been accepted as the method of choice by most of the authors for open long bone fractures caused by missiles and fire-arms.

The classification of open fractures was proposed by Gustilo etal[1] in 1976. In a later classification 1984 Gustilo[2] divided the more severe Type III fractures into three sub-types in the order of worsening prognosis.

Type III a -Extensive soft tissue laceration or flaps or wounds of high energy trauma but with adequate soft tissue to cover the fractured bone.

Type III b - Wounds with extensive soft tissue injury or loss with periosteal stripping or bone exposure.

Type III c- Open injuries associated with arterial injuries requiring repair.

Most reported series of open fractures have focussed their attention on tibia with small number of Type III fractures. We present our observations on the management of 30 patients with Type III open fractures of long bones caused by high velocity bullet injuries stabilized primarily with external fixator. The purpose of this report is to examine our experience with these injuries and to analyse various factors contributing to major complications.

Materials and methods

The results of a prospective study of the treatment of open long bone fractures caused by fire-arms, by external fixator are presented The study was conducted on 30 Type III open fractures between January 1992 to June 1994 in the orthopaedic unit II of the Govt. Hospital for Bone and Joint Surgery, Barzulla, Srinagar.

There were 26 male and 4 female patients with an average age of 24 years (8-60 years). Table I. The bones involved are shown in Table II.

The patients were initially treated with thorough excision of the dead and devitalized tissue and copious saline irrigation and stabilization with external fixation device, either unilateral or bilateral, depending on the bone involved and the choice of the surgeon. The patients were put on prophylactic I/V antibiotics (cefazolin and gentamcin) for a period of one week and oral cefazolin for a further period of two weeks. Attempts were made to cover the fracture site primarily with soft tissue which was mobilized locally. 22 of the patients in whom the exposed bone could not be covered with soft tissue were allowed to granulate for a period of 3-6 weeks and were later covered by local fascio-cutaneous or myo-cutaneous flaps by plastic surgeon. Cortico-cancellous bone grafting was done in 14 patients (3 Type IIIa, 11 Type IIIb) and centralization of ulna was done in one patient with comminution and bone loss of distal radius. The follow-up average 15 months (4-30 months).

The patients were followed till union, established non-union or amputation. Amputations performed within 6 months were labeled as early secondary amputation and those performed after 6 months were defined as late secondary amputation. Out of 4 amputations performed

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2 were early secondary amputations and 2 were late secondary amputations. The duration of the external fixator was based on the state of the soft tissue healing and bone union. In Type III a fractures the fixator was removed in 6-12 weeks and in Type III b fractures the fixator remained for 10-20 weeks which was followed by P.O.P cast till complete union.

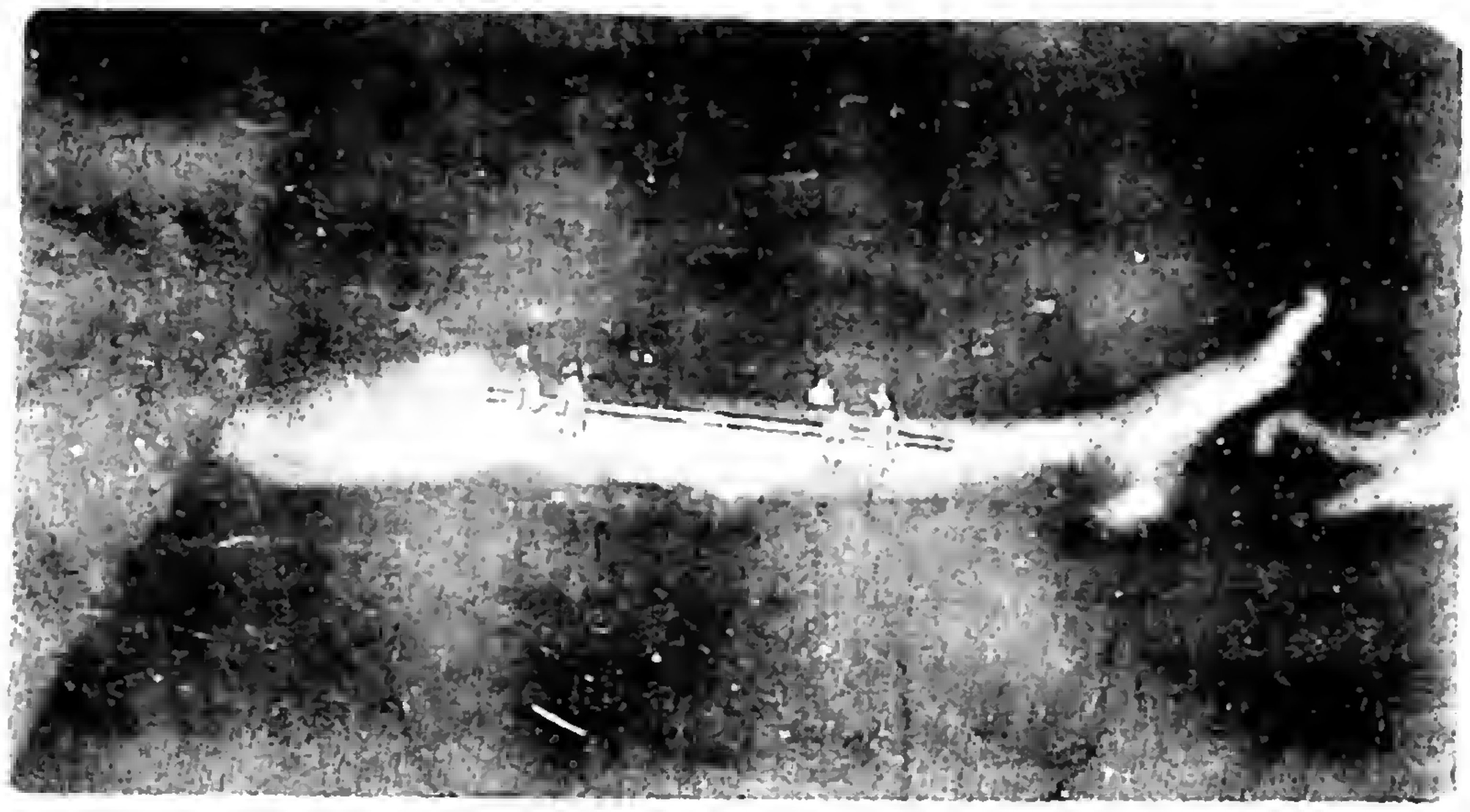

Fig I: Clincial Photograph of external fixation.

Results: Table III.

Type III a fractures:

There were 8 Type III a fractures. All fractures were primarily stabilized with external fixator. Out of these, 5 fractures united within 12 weeks and 3 required cortico-cancellous bone grafting to facilitate union. All of these fractures eventually united within 30 months. In all three patients the skin defect was covered within one week of injury. At final follow up there were no infections, joint stiffness or amputations. However, one patient united in malreduced position i.e., significant recurvatum of the tibia.

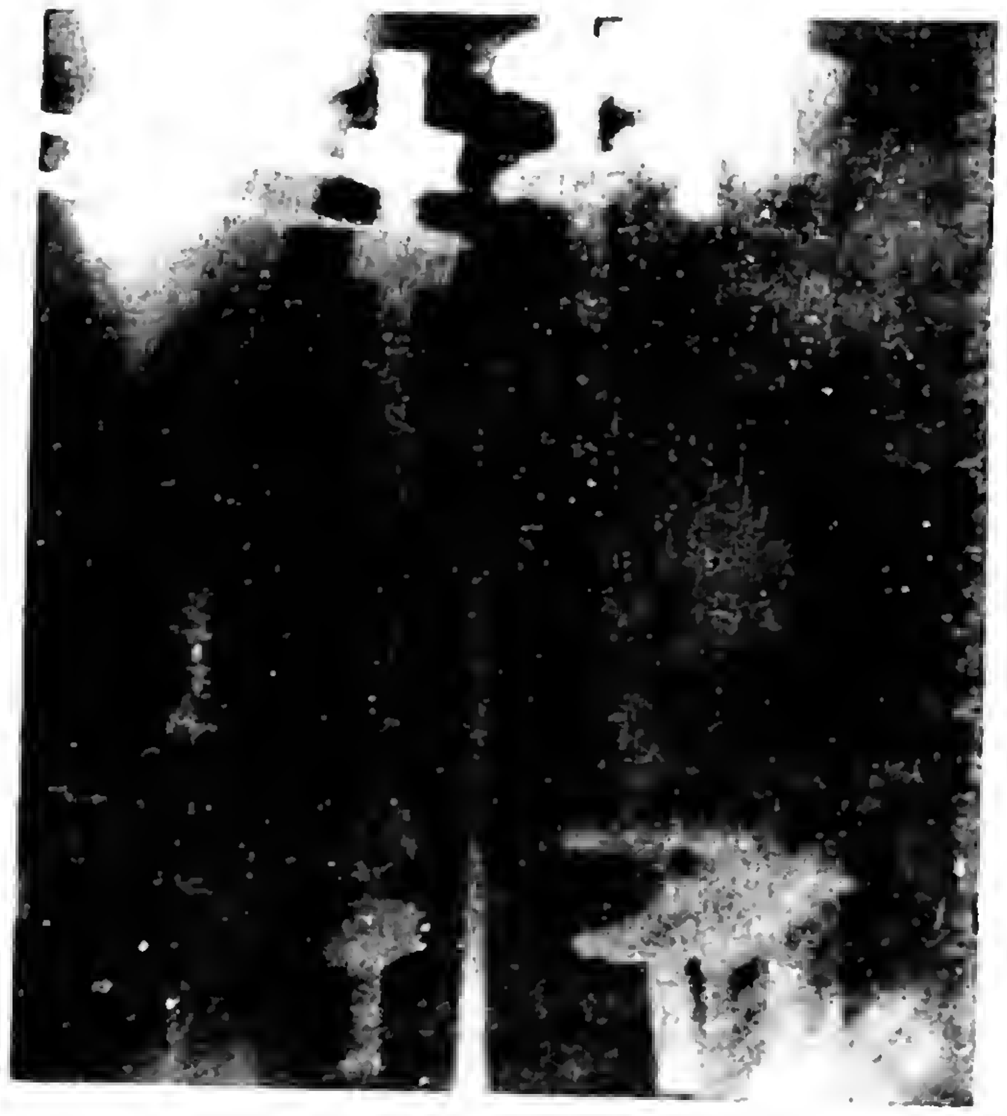

Fig II: X-ray of the external fixation.

Type IIIb fractures:

22 patients in this group were studied. Wound coverage was achieved between 3-6 weeks of injury by plastic surgeon, including cross leg flap in 8, posterior tibial artery based flap in 4, local rotation flap in 4, abdominal flap in 2 patients. Secondary amputation was done in 4 patients (3 below knee and 1 above knee) one month after surgery due to intractable infection, extensive tissue damage and laceration of posterior tibial nerve with anaesthetic foot. 6(33%) patients developed deep wound infection which was eventually controlled and they did not require amputation. Bone grafting was done in 11 patients in an average time of 15 months (6-30 months). In the 12th patient centralization of the ulna was done because of severe comminution and bone loss at the distal radius. Fibular graft supplementation of the tibial defect was required in 2 patients in addition to corticocancellous bone grafting. 68% of the patients had residual joint stiffness at final follow-up. However, this did not impair their routine activities significantly.

Fig III: Final Result.

Discussion:

The management of fire-arm injuries of the limbs poses considerable difficulties. Significant comminution of the bones associated with considerable soft tissue damage requires some form of fracture stabilization which is rigid and at the same time allowing adequate soft tissue management. Sophisticated multiplane external fixator has already established a firm place for itself as a method of treatment for open fractures of long bones in advanced society. It is known to allow direct wound care while maintaining the fracture is satisfactory alignment during the initial weeks of bone healing and at the same time allowing joint mobilization. However, in Kashmir the bulk of such patients are from low socio-economic background and also because of the heavy rush of patients with fire-arm injuries the fixator must be of a simple design which is readily available and easy to use. In our experience with open type III fractures external fixation was the treatment of choice for fracture stabilization and wound care because the subsequent soft tissue coverage was easy. There were 2 cases (6%) of pin tract infection but they were mild and treated successfully.

Many of these patients required secondary soft tissue procedures in the post operative period. The sub-classification of Gustilo[2] has been found to be appropriate regarding the prognosis of these injuries.

Type IIIa fractures had a non-union rate of 37%. There was no deep infection and no secondary amputation was required. Type IIIb fractures carried a significantly worse prognosis not only regarding time to union but also infection and rate of amputation. In the present series type IIIb fractures had 60% non-union rate. 33% patients developed deep infection and 18% had to undergo secondary amputation. These results are higher than that of Caudle[3] and could be attributed to primary bone loss involved with high velocity bullet injuries. Our results confirm the observations of other authors[4] about the role of soft tissue in the healing of fracture which form the rationale of early aggressive soft tissue reconstruction around the fracture site.

Table - I Age and Sex distribution

Age in years	Male	Female	Total
5 - 10	0	1	1
11 - 20	3	2	5
21 -30	15	0	15
31 - 40	3	0	3
41 - 50	3	0	3
51 - 60	2	1	3
Total	**26**	**4**	**30**

Bone grafting was performed more than 6 weeks after the soft tissue cover was obtained. Complications in the present series included pin tract infection, osteomyelitis at fracture site and mal-union. 5 of the type IIIa and type IIIb fractures were not adequately reduced at the time of application of the fixator and eventually all united in mal reduced position. 2 patients developed limb length discrepancy of 1.5 cm and 2 cm respectively. 2 patients developed angulation after the removal of the fixator. This stresses the need to retain the fixator for longer period of time.

The overall results compare well with those of other series of (Caudlle and Stern[3].

We consider that simple external fixator and early aggresive soft tissue reconstruction gives good results provided the surgeon understands the basic principles of external fixation so that it can be judiciously used when the need arises.

Table - II: Involvement of Individual Bones

Bone Involved	No. of Pts.	Primary Union	Non-union	Infection	Amputations
Tibia	16	8	3	4	3
Femur	6	1	5	[illegible]	[illegible]
Humerus	6	4	2	2	[illegible]
Ulna	1		[illegible]		
Radius	1	[illegible]			
Total	30	13	[illegible]	[illegible]	[illegible]

Table - III

Type of Fracture	No. of Fractures/ Patients	No. of No-unions/ Fractures	Infections/ Fractures	No. of Secondary Amputations
IIIa	8/8	3/8(37%)	[illegible]	0
IIIb	22/22	12/20* (60%)	[illegible]/22 (33%)	4/22 (18%)

Note: Group IIIc cases were not involved in the study as almost all required amputation primarily.

** : Two patients had to undergo early secondary amputation.*

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SIGNIFICANCE AND ASSESSMENT OF WIDAL'S REACTION IN THE DIAGNOSIS OF TYPHOID FEVER IN KASHMIR:

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Abstract: *Serum samples of 6365 suspected enteric fever patients were subjected to slide and tube agglutination tests for detection of S. typhi flagellar 'H' and Somatic 'O' antibodies. Standard Widal test was used for tube agglutination. Sera of 1550 (24.4%) showed significant antibody titres of 1:160 and 1:180 with flagellar 'H' and somatic 'O' antigens.*

560(36%) of the positive samples showed a titre of more than 1:160 and 1:180 with flagellar 'H' and somatic 'O' antigens respectively, where as rest of 995 (64%) samples depicted titres of 1:160 and 1:180 for 'H' and 'O' aggluntinins.

Eighty percent bacteriological proven cases of typhoid showed a significant titre with widal. High sensitivity of 69.2% was noticed for flagellar 'H' antibodies as compared to 56.9% for somatic 'O' antibodies. Positivity of widal was highest in 1998 which coincided with emergence of multidrug resistant S. typhi strains in Kashmir. Although culture positivity is the gold standard for diagnosis of typhoid fever, widal positivity shows sensitivity and correlation of the test in such type of cases. Even if widal reaction has certain limitations in endemic areas like Kashmir, it should not cease to be used especially when sensitivity seems to be higher for 'H' antibodies.

Key words: *S. typhi, Widal, Somatic, Flagellar, agglutinin, titre*

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Introduction

Salmonella typhi is a gram-negative facultative intracellular pathogen that multiplies in the phagoocytic cells of reticuloendothelial system. Macrophages play an important role in clearing the bacterial load during acute infection[1]. The role of humoral and cell mediated immune mechanisms in strengthening these innate cellular responses, in offering protection against infectioon by Salmonella typhi is not clear.

Typhoid fever caused by Salmonella typhi is an endemic infectious disease in many parts of India. It poses an important public health problem on account of its morbidity and mortality, development of carrier stage, relapse, reinfection and multidrug resistance that are associated with this disease. To study the required immune mechanisms in individuals suffering from infection, antibody titres to flagellar 'H' and somatic 'O' antigens of S. typhi are determined by widal test. The widal test introduced by Widal, Sicard and Grunbaum in 1896 is in use now for more than one century[2-3]. Although controversies still exist due to several factors like high endemicity, antigenic cross reactivity with other agents, previous vaccination, non-availability of paired sera, poor standardized reagents, diverse methods and criteria of interpretation[4-8].

Rising antibody titre for widal in paired sera has been traditionally considered as a good diagnostic test but today it seems to be impracticable. A two-fold increase in titres after 4 weeks may help in confirming the diagnosis. Since isolation rates of Salmonella typhi from cultures may not exceed 50%[9] because of prior antibiotic therapy, the diagnosis largely depends upon clinical features and serological tests. Detection of Igm antibodies to S. typhi is a useful adjunct to the existing tests as can presumably indicate a recent or ongoing infection[10].

In Widal test, suspensions of killed S.typhi, specially prepared for: (1) the detection of antibody reacting with the falgellar 'H' antigen 'd' and; (2) the somatic 'o' antigens 9 and 12 are used.

Any organism in the genus Salmonella possessing 'H' antigen 'd' or 'O' antigens 9 and 12 is capable of stimulating the immune mechanisms of its host to produce antibodies against these antigens in addition to antibodies against any other antigens it may possess. In 1969, the Kauffman White scheme which classifies Salmonella by their somatic and flagellar antigens included 97 Salmonellas possessing flagellar antigen 'd'. Of these, however, only 8 including S.typhi possessed somatic antigen '9' and only 6 including S.typhi possessed somatic antigen '12'[11].

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Salmonella infections have caused great concern in recent years due to emergence of plasmid mediated multidrug resistant strains globally[12]. Though ciprofloxacin is an effective drug for treating enteric fever, the high cost of drug may lead to irregular treatment and thus treatment failure in many patients. Further as fluroquinolones in general are contraindicated in children, selection of appropriate drug for treating resistant typhoid in children becomes all the more important.

Table-1: Anti S. typhi 'O' and 'H' agglutinins among healthy donors. (n=100)

Antigen	No. of positives	Percentage
	cutt off$\geq$ 1:80 'O' agglutinins $\geq$ 1:160 for 'H' agglutinins	
S. typhi'O'	03	03
S.typhi 'H'	02	02
S.typhi 'O' and 'H' both	02	02
Total	**07**	**07**

Material and Methods

Classic slide and tube agglutination tests were performed as described by Widal[2] for analysing the serum samples of 6365 suspected cases of enteric fever consisting of 3955 adults and 2410 children, attending the Sher-i-Kashmir Institute of Medical Sciences, Srinagar, over a period of 5 years (1995-1999). Patients having continuous fever for 3-15 days suspected to have typhoid were included in the study. Serum samples were by and large collected in 2nd week of fever. 5ml venous blood was collected from time to time and examined as soon after collection as possible. Where delay occured, sera was kept at-20°C in small aliquots till used. Before use, each sample was inactivated at 56°C for 30 minutes.

Somatic and flagellar antigens of S.typhi were used for determining the antibody titre. Antibody titres for somatic 'O' and flagellar 'H' antigens measuring 1:180 and 1:160 respectively were considered positive for Widal's test.

Table-2: Widal positivity among patients suspected to have typhoid fever.

Year	Total no.	+ve	%	Adults no.	+ve	%	Children no.	+ve	%
1995	1300	332	25.5	780	202	25.8	520	130	25.0
1996	1180	287	24.3	690	205	29.7	490	82	16.7
1997	1323	276	20.8	870	196	22.5	453	80	17.6
1998	1286	355	27.6	820	286	34.8	466	69	14.8
1999	1276	305	23.9	795	255	32.0	481	50	10.3
Total 1995-1999	6365	1555	24.2	3955	1144	28.9	2410	441	18.2

One hundred samples consisting of healthy blood donors and hospital personnel were also included in the study as controls. None of the patients and controls gave any history of previous typhoid attack or TAB vaccination.

Table-3: Widal test results for bacteriologically proven cases of typhoid (1995-99)

Group	No. of sera	Cut-off tire 'O' (1:80)	'H' (1:160)
Children	20	12 (60%)	15 (75%)
Adults	45	25 (55.5%)	30 (66.6%)
Total	65	37 (56.9%)	45 (69.2%)

Figures in parenthesis are percentages

Rapid Slide Test

50ul drops of S.typhi 'O' and 'H' antigens were mixed with 20, 10 or 5ul of serum over the glass slides and agglutination reactions were read within 2 minutes.

Table-4: Frequency of antibodies against S.typhi in normal population from across India.

Year	Worker	Cut-off	Widal percent positive 'O'	'H'
1962	Singh and Nair Pondichery (18)	1:50	20:1	12:9
1964	Singh Delhi (19)	1:50	12:5	21
1966	Khan et al. Lucknow (20)	1:20	20	28.5
1988	Joshi et al Gujrat (21)	1:80	0.9	1.1
1990	Cherium et al Vellore (22)	1:80	5.3	0.9
1991	Divangyam et al Madras (9)	1:100	3	2.8
1993	Raisaly et al Calcutta (23)	1:160	1.8	
1996	Sunjay Shukla (14)	1:80	13.8	8

Tube Agglutination Test

Tube test was carried out using S.typhi flagellar 'H' and somatic 'O' suspensions prepared in our laboratory as per standard reference technique[13]. Doubling dilutions of patients serum were made in 0.85% saline starting from 1:20. Volumes of 0.2ml of each dilutlion were placedin round bottomed agglutination tubes (7.5cm x 1cm) for 'O' antigen suspensions and in Dreyer tubes for 'H' antigen suspensions. An equal volume of appropriate antigen was added to each tube to give final serum dilutions from 1:40 upwards. All tubes were incubated in a water bath at 56°C for 4 hours, removed and left at room temperature overnight before the final readings were taken. Each test sample batch was put alongwith positive and negative control to reduce the margin of technical error. A titre of 1:180 for somatic 'O' antigen and 1:160 for flagellar 'H' antigen was taken as positive. The agglutination reactions with 20, 10 or 5ul of serum were shown to correspond with the tube widal titres of 40, 80 or 160 respectively as has been described earlier also[14].

Blood Culture

The requests for blood culture were received only from 1330 patients. Standard cultural procedures were performed to isolate Salmonella from these cases. For cultures 5ml blood was collected aseptically in glucose broth containing 0.05 percent liquoid. Incubation at 37°C for seven days with subculture on alternate days was made. The suspected colonies were identified by standard biochemical and sero-agglutination reactions.

Results

The basal antibody levels to S.typhi antigens among normal healthy population, suspected patients and bacteriologically proven cases are reported in Table 1, 2 and 3 respectively.

Seven percent of normal healthy population in the area had antiboody titre of 1:80 and 1:160 for 'O' and 'H' agglutinins respectively. Since these values are closer to widely accepted antibody cutoff of 1:80 or more, we also interpreted our results taking cut off of 1:180 for 'O' somatic and 1:160 for flagellar 'H' agglutinins respectively. Sera of 1550 (24.4%) significant titre cases showed titres of 1:160 and 1:180 with flagellar 'H' and somatic 'O' antigens respectively.

Five hundred and sixty (36%) among positives depicted a titre of 1:160 and 1:180 for 'H' and 'O' agglutinins, whereas, rest of 995 (64%) positive samples showed titres of 1:160 and 1:80 for 'H' and 'O' agglutinins respectively.

Although culture positivity is the gold standard for diagnosis of typhoid, Widal positivity shows sensitivity and correlation of test in such type of cases. Sensitivity seems to be higher for 'H' antibodies. Overall sensitivity in our study was found to be 56.9% for 'O' and69.2% for 'H'antibodies. Positivity for Widal was highest - 34.8% for adults in 1998 which coincides with the emergence of multidrug resistant S.typhi strains in Kashmir at that time[15].

Discussion

Serological studies by Widal have certain limitations in endemic areas like Kashmir but it should not cease to be used on account of wide difference in their cut off values. In present study cut off titre 1:160 for 'H' agglutinins and 1:80 for 'O' agglutinins showed 80% sensitivity among the culture positive typhoid patients. Currently neither the doctor nor the patient would like to wait for two weeks before initiating antibiotic therapy and in that case the diagnostic utility of Widal is bound to be limited. In 65 bacteriologically confirmed typhoid cases, significant widal titre was seen in 52(80%) patients. Rattan et al[16] and Neeraj Jindal[17] also found similar correlation while comparing culture with serologic tests in typhoid fever cases. Sensitivity of Widal is lower for antibody levels in the first week of illness and in such situations rise for 'H' antibodies is found useful and should not be underscored. Updated data on the basal antibody titres in various regions is essential for deciding the cutoff level and interpretation of Widal test. Data on the prevalence of antibodies to 'H' and 'O' antigens of S. typhi in normal population at various places in India is shown in Table 4.

In present study sensitivity seems to be higher for 'H' antibodies. Overall sensitivity found was 56.9% for somatic 'O' agglutinins and 69.2% for flagellar 'H' agglutinins at cut off titre of 1:80 and 1:160 respectively.

Most of patients in this study had received antibiotics before the sera was drawn which could well be the reason for receiving lesser number of samples for bacteriological cutlure.

With heavy antibiotic usage the problem of drug resistance especially to chloramphenicol, cotrimoxazole, ampicillin and recently to ciproofloxacin may pose a challenge in future. The greater positivity for Widal in 1998 could well be due to the outbreak of multidrug resistant S.typhi in Kashmir at that time.

Percentage positivity of 28.9% in adults was quite high as compared to that of 18.2% in children. As enteric fever outbreaks usually occur in summer months in Kashmir, our study cases were also mostly distributed in summer season.

Calibration of slide test in tune with the tube test made it to correlate well with the latter.

Addition of 2-mercaptoethanol by some workers to serum samples[10] for diagnosis of IgM antibodies of typhoid fever in the first week of illness has shown increase in sensitivity of test from 84% to 90% with 100% specificity. This modified Widal test seems to be the test for future as it will prove cost effective and less cumbersome as compared to ELISA, crossed immuno-electrophoresis and RIA.

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CHANGING PATTERN OF DRUG RESISTANCE IN ESCHERICHIA COI CAUSING URINARY TRACT INFECTION

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Abstract: *This study was carried out to find the changes in the pattern of drug sensitivity to Escherichia coli causing UTI over a period of seven years. The study comprises of prospective data from Sept. 1990 to Sept. 1992 and again from January 1997 to August 1997. E. coli is the commonest cause of UTI comprising 72% of the total isolates. Two hundred urinary isolates of E. Coli were studied for sensitivity pattern by Kirby Baeur method. 90% of E. coli are still sensitive to antimicrobials like cefotaxime, gentamicin, amikacin and nitrofuratoin while as 90% of them have developed resistance to drugs like amipicillin, amoxycillin, co-trimoxazole, ciprofloxacin, norfloxacin, nalidixic acid, the resistance of quinolones having risen maximally from 10% (1992) to 90% (1997). This high percentage of increase in resistance to quinolone can be attributed to irrational and over the counter use of quinolones.*

Key words: *Escherichia coli, Urinary Tract Infection, Drug Resistance*

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Introduction

Escherchia coli is the most common cause of urinary tract infection and is capable of causing a wide range of illness ranging from uncomplicated urethritis to symptomatic cystitis, pyelonephritis and sepsis[1]. The objective of antimicrobial therapy is to eliminate bacteria from the unrinary tract. Selection of an appropriate antimicrobial has become complex, because of increasing number of compounds available, each with its characteristic spectrum. The emergence of antibiotic resistant bacteria has generally correlated with the rise and fall of specific antibiotic use in clinical practice. The decline in the susceptibility of E. coli to various related antibiotics has been noted in the recent few years in the different studies which have been conducted[2]. In our study we have compared the antibiotic resistance of E.coli causing urinary tract infection studied between 1990-1992 to that observed in another study conducted between Feb. 1997 to August 1997. We have noted a changing pattern of antibiotic resistance in E. coli causing UTI over a period of seven years especially to quinolones.

Material and Methods

The patients were selected from among the medical OPD and also the inpatients of the Sher-i-Kashmir Institute of Medical Sciences In the first part of the study conducted between 1990 to 1992, 100 urinary E. coli isolates were subjected to study and in the second part of the study (Feb. 1997 to August 1997) 100 Ecoli Lsolates were studied. Mid stream specimen of urinar was collected in a sterile container and subjected to routine urine culture and confirmation done by biochemical tests. Antibiotic sensitivity of E. coli to various antimicrobials belonging to following six broad group was determined:-

1. Quinolones : Norfloxacin, ciprofloxacin, nalidixic acid
2. Aminoglycosides : Amikacin, gentamicin
3. Cephalosporins : Cephalothin, cefotaxime
4. Pencillins : Ampicillin
5. Sulphonamides : Co-trimaxazole
6. Nitrofuran compounds : Nitrofurantoin

Concentration of the antibiotic discs used was as follows:-

Ampicillin (25ug), gentamicin (10ug), Nitrofurantoin (100ug), Nalidixic acid (30ug), Co-trimoxazole (25ug), amikacin (30ug), cephalothin (30ug), cefotaxime (30ug), norfloxacin (10ug), ciprofloxacin (5ug). Kirby Bauer method was used to determine the sensitivity of E.coli to various antibiotics (as recommended by NCCLS 1975). Interpretation was done by reference to table of zone-size interpretative chart for Kirby Bauer method.

Result

From our observations it was noted that E. Coli continues to be the most common cause of urinary tract infection comprising from 68% to 70% of the total isolates

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causing UTI.

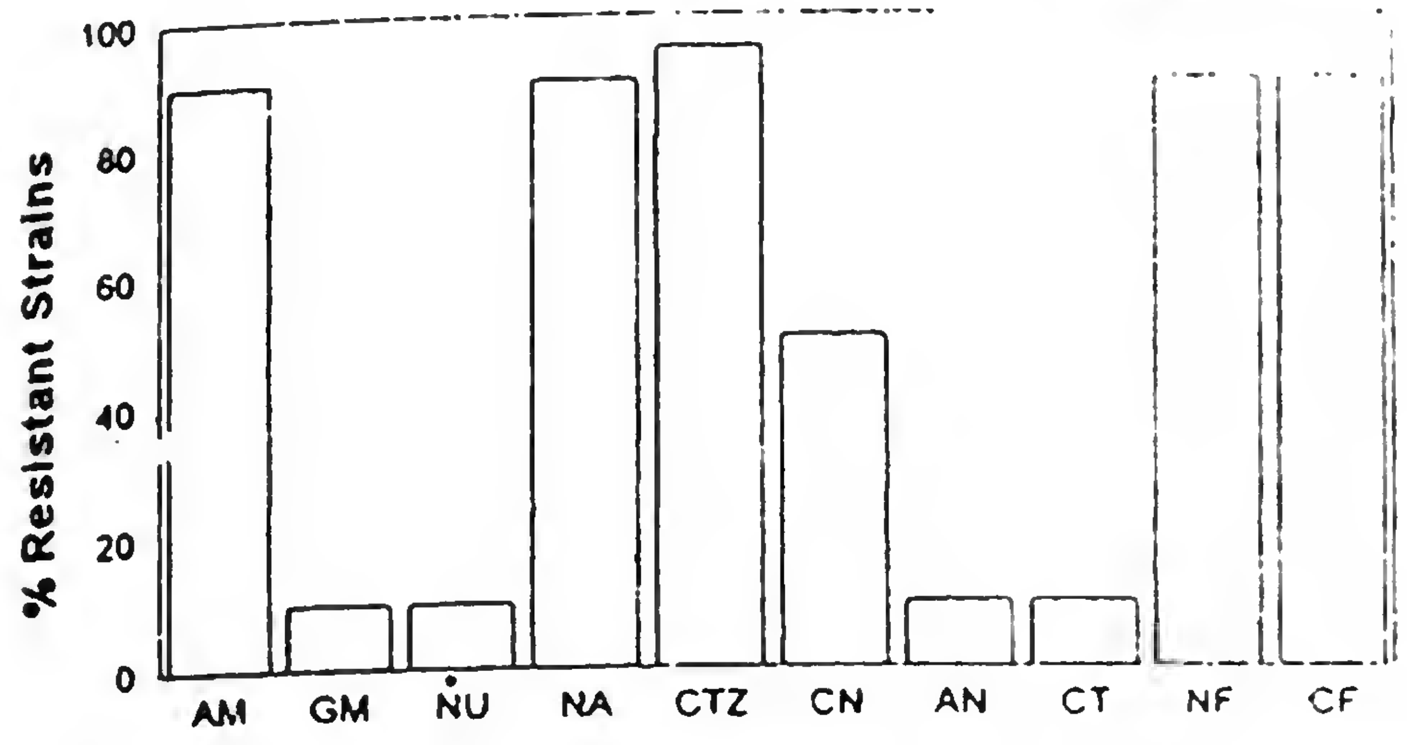
Table 1: Resistance of Escherichia Coli urinary isolate to individual drugs

(Feb 1997 - August 1997)

Antimicrobial Agent	Total strains	No. of strains resistant	% age of resistant strains	No. of resistant sensitive	%age of sensitive strains
Ampicillin	100	90	90	10	10
Gentamycin	100	10	10	90	90
Nitrofurantoin	100	10	10	90	90
Nalidixic acid	100	90	90	10	10
Co-Trimaxazole	100	95	95	5	5
Amikacin	100	10	10	90	90
Cephalothin	100	55	55	45	45
Cefotaxime	100	10	10	90	90
Norfloxacin	100	90	90	10	10
Ciprofloxacin	100	90	90	10	10

Fig: I:

Feb. 1997 - August 1997



Resistance of E.coli isolates from urine of UTI patients to various antimicrobials

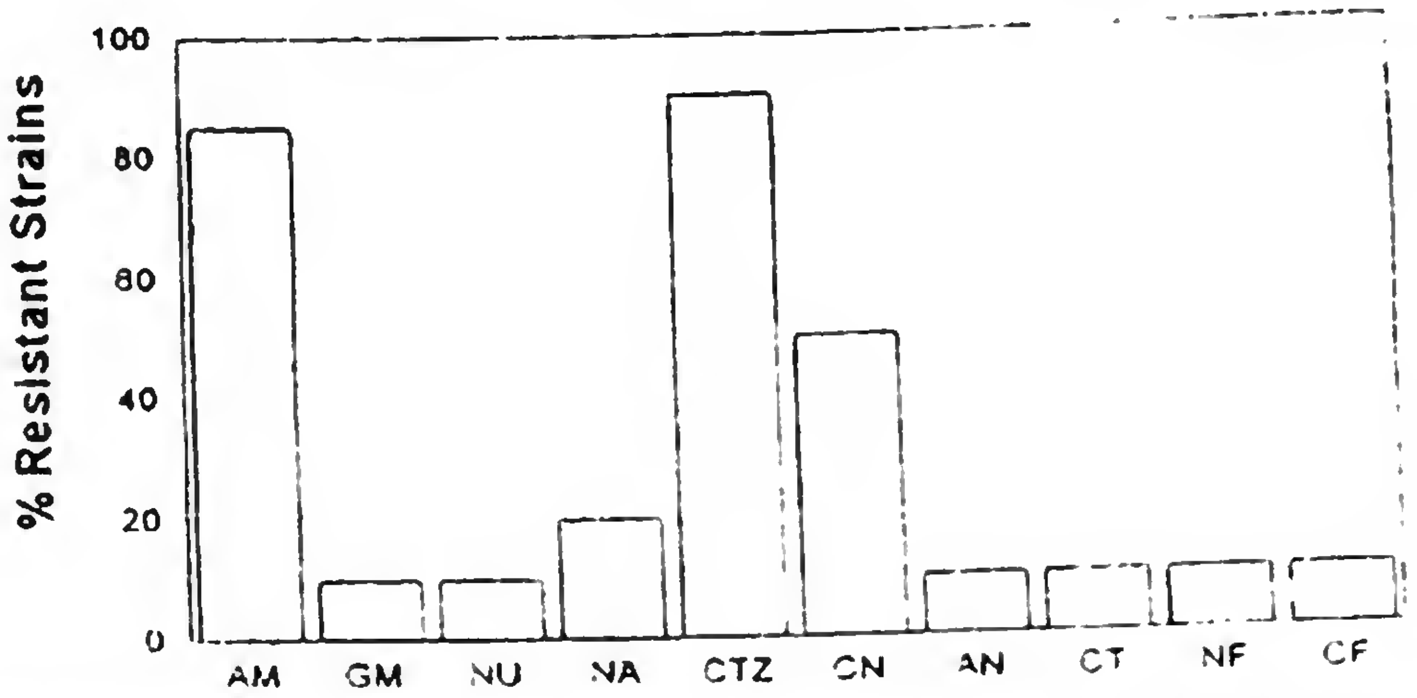
AM - Ampicillin
GM - Gentamycin
NU - Nitrofurantoin
NA - Nalidixic acid
CTZ - Co-Trimaxazole
AN - Amikacin
CN - Cephalothin
CT - Cetotaxime
NF - Norfloxacin
CF - Ciprofloxacin

In our recent study 90% of the isolates were found resistant to norfloxacin, ciprofloxacin, nalidixic acid, ampicillin and 95% to co-trimoxazole while as only 45% show sensitivity to cephalothin. In the same study 90% of the isolates were found sensitive to cefotaxime, gentamicin, amikacin, and nitrofurantoin (Table i and Fig. ii).

In the previous study (1990-92) 10% of the isolates had been found resistant to norfloxacin, ciprofloxacin, cefotaxime, amikacin, nitrofurantoin, gentamicin while as resistance to ampicillin, cotrimoxazole was noted in 85% and 90% respectively while as resistance to nalidixic acid and cephalothin was noted in 20% and 50% respectively (Fig. 2).

Fig: II:

1990 - 1992



Resistance of E.coli isolates from urine of UTI patients to various antimicrobials

AM - Ampicillin
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CT - Cetotaxime
NF - Norfloxacin
CF - Ciprofloxacin

Discussion

The rising incidence of resistance in E.coli to most antimicrobials has been noted in most parts of the world. Grunberg (1984) studied E. coli from urinary tract infection during 1971-1982 and found a gradual increase, in the percentage of resistance to ampicillin, sulphonamides, tetracycline and trimethoprim over the years[2]. Moreover the incidence of resistance has been found higher in developing countries as compared to that in developed countries[3,4]. In a study conducted in India by Diwan and Sharma (1978) on E. coli urinary isolates, 81% of the strains were found to be resistant to ampicillin while as in another study conducted by Ansari (1981) it was found that the resistance to ampicillin in E. coli was 44.5% only[5,6]. This could be attributed to the fact that only 70% of the E.coli isolates, were from UTI patients in the study conducted by Ansari et al. In our present study in Kashmir valley a high level of resistance to ampicillin and co-trimoxazole noted in 1990 being 85% and 90% respectively, has further risen by 5% in each case over a period of seven years. The level of resistance to aminoglycoside which was low at 10% continues to be same over a period of 7 years. This again could be attributed to less use of parenteral aminologlycosides as compared to the other more feasible orally consumed antibiotics.

In the first generation cephalosporins like cephalothin the rise in the resistance is only 5% being 50% for cephalothin in 1997. The third generation cephalosporins like cefotaxime are still effective as the 90% of the isolates are still found sensitive as in the previous study in 1990-92, thus, showing no increase in resistance over the past seven years

But a sharp rise in the percentage of resistance of E.coli to quinolones like norfloxacin and ciprofloxacin has been noted. The resistance has risen from 20% to 90% in case of nalidixic acid and from 10% to 90% in case of norfloxacin and ciprofloxacin over a period of seven years. In a recent study in 1997 a similar high level resistance in pseudomonas aeruginosa against fluoroquinolones has been noted. This indicates that resistance to fluoroquinolones is on increase among bacteria[7].

The drastic rise in resistance of E.Coli to quinolones could be attributed to irrational and over the counter use of quinolones during the recent few years which has led to selective pressure in E.coli. In a pediatric unit in Tokyo, an increase in the resistance in E. coli to trimethoprim, sulphamethoxazole, ampicillin and cephalosporin was noted as each of the drug was introduced[8].

Thus there is correlation between the utilization of an antibacterial drug to the occurrence of resistance to this drug among the pathogenic bacteria isolated from the urine samples from sample population, as seen in 1970 in Switzerland from the data from continuous monitoring of OPD prescriptions among the inhabitants[9].

Thus we conclude that there should be rational use of antibiotic to prevent or diminish the rate of development of resistance to antibiotics. The use of synergistic combination of antimicrobials to treat infections due to resistant or relatively resistant micro-organisms, are also useful in countering the resistance of micro-organism.

Moreover antibiotic policy and procedures should be followed by physicians for the firt choice of antibiotic.

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CYSTS OF HEAD AND NECK REGION. (REVIEW OF 110 CASES)

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Abstract: *110 cases of cystic lesions in head and neck region reported from January to December 1995 (Both inclusive), were reviewed and analysed. They included 51.8 percent epidermal inclusion cysts, 15.6 percent dermoid cysts, 13.5 percent thyroglossal cysts, 11 percent branchial, 4.5 percent mucocoele and 3.6 percent lymphatic cysts.*

Key words: *Benign Cysts, Cystic Lesions; Head and Neck Masses; Congenital Cysts.*

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Introduction

Different types of cysts are encountered in the head and neck region. Congenital cysts constitute 3 percent of masses in this region[1]. Cystic degenerations of colloid goiter is commonest type of benign cyst reported[3]. Midline congenital cysts include dermoid and thyroglossal cysts and lateral to midline is branchial cyst which results from failure of primordial branchial cleft to get closed.[3,4]

Material and Methods

110 benign cystic lesions situated in head and neck area, were studied by FNAC in cytology sections of pathology Department, Govt. Medical College Srinagar in the period from first January to ending December 1995. The cytological material was obtained with help of 20ml disposable syringes. Smears fixed in methanol (Absolute) were stained with maygrunwald-Giemsa and Haematoxylin -Eosin Stain.

The cytological diagnoosis were confirmed on histopathology of excised specimen. The age varied between 1 year to 70 years. The cysts of thyroid gland are not included in this study as they are being discussed in a separate study. Malignant cystic lesions are also not included in the study.

Results:

For the type and frequency of lesions see table.

Epidermal inclusion cysts and dermoid cysts yielded brownish pultaceous material and smears on cytological examination granular amorphous debris, nucleated squamous cells with plenty of eosinophilic cytoplasm, moderate to dense aggregate of neutrophils in most of cases and cholesterol crystals in 3 cases which on histology were subtyped as tricheliminal cysts.

Thyroglossal cysts on aspiration yielded clear fluid and smears from centrifuge deposits showed mostly squamous cells (11 of 15 cases) and columnar epithelium in 4 cases. Lymphocytic infiltrates were seen in 3 cases. Thick pus like fluid was aspirated from the cysts diagnosed as branchial cysts. The cytological examination of smears from these cysts showed anucleate keratinized cells, squamous cells of variable maturity against a background of amorphous debris. Lymphatic cysts yielded clear fluid and smears showed numerous lymphocytes against an amorphous background.

Table showing type and frequency of benign cystic lesions of Head and neck

S.No.	Lesions	Total	Percentage
1.	Epidermal inclusion cysts	57	51.8
2.	Dermoid cysts	17	15.6
3.	Thyroglossal cyst	15	13.6
4.	Branchial cysts	12	11.8
5.	Mucocoele	5	4.5
6.	Lymphatic cyst	4	3.5
	Total	**110**	**100**

Mucocoeles though clinically presented with firm nodules of varying sizes from .5 to 2.5 cms mostly around theoral cavity on aspiration yeilded thick mucoid material and smears showed mucin filled macrophages (Mucinophages) against thick amorphous background.

Discussion:

Cysts are met with in many pathological conditions and term applied clinically should refer only to those swellings in which there is collection of fluid or semisolid material in a sac that has lining membrane, 110 such cases

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were reviewed in this series. They included 51.8 percent epidermal inclusion cysts, 15.6 percent dermoid, 13.6 percent thyroglossal, 11 percent branchial, 4.5 percent mucocoele and 3.6 percent lymphatic cysts. In a similar study Couto et al[2] reported that thyroid cyst (Cystic degeneration)comprised 78 percent series and others included, branchial cysts 2.2% lymphatic cysts 1.7%, epidermal inclusion cysts 13%, dermoid cysts 1.7%and metastatic squamous cell carcinoma in lymph node with cystic degeneration 3.4% of the series. Bhaskeran et al[5] describerd epidermal cysts comprising 15.2%, dermoid 3.4percent and thyroglossal cysts 6.2 percent of all the cystic lesions in head and neck region. Dejmek et al[6] reported lymphatic cysts forming 1.7 percent of series. Apparently there is gross disparity between figures given by these authors and our observations which is mainly due to the fact that we have not included cysts of thyroid gland and malignant cysts of the region in this series as they are to be discussed in separate study. If we include these two types of lesion from the series described above our figures come in approximation with their observations.

The differentiation of epidermal cysts from dermoid cyst is purely based on the clinically midline location of latter, as cytology of both types is similar. Congenital cysts were common in younger age groups.

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NEONATAL POYCYTHEMIA COMPARISON OF PARTIAL EXCHANGE TRANSFUSION WITH PLASMA VERSUS NORMAL SALINE

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Abstract: *Polycythemia occurs frequently in neonates. A prospective study was conducted over last one year to evaluate the efficacy and safety of partial exchange transfusion with plasma versus normal saline in polycythemic babies. Out of 500 admissions to the neonatal unit; polycythemia was detected in 26 (5.2%). Seventeen babies (66%) were appropriate for dates and nine (34%) were small for dates. Twelve babies (46%) were preterm and 13 (50%) were term and one (4%) was post term. Four (15%) were twin deliveries. Symptoms suggestive of polycythemia included respiratory distress 67%; Jitteriness 34%; lethargy 24%; jaundice 19% and refusal of feeds 15% Hypoglycemia was seen in 19% babies.*

Babies were randomly assigned to receive partial exchange blood transfusion (PEBT) with either normal saline or plasma. Both groups were comparable in terms of birth weight; gestational age and pre-exchange hematocrit (Hct). A significant fall in hematocrit was noticed at 6 hours following PEBT which persisted even at 24 hours ($p<0.05$) for both groups.Majority of babies became asymptomatic within 24 hours after PEBT. No complications related to the procedure were encountered in the two groups.Partial exchange with normal saline is as effective and safe as with plasma in polycythemic newborns.

Key words: *Polycythemia; Hematocrit; Partial Exchange Transfusion.*

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Introduction

Polycythemia in neonates is a common problem with a reported incidence of 0.4 - 4%[1]. It may cause serious insults to brain, heart, kidneys, lungs and intestines[2-4]. Symptoms in polycythemia are related to increased blood viscosity and decreased blood flow to various organs. Babies with symptomatic polycythemia are often subjected to partial exchange blood transfusion (PEBT) either with plasma or normal saline[5]. Plasma is known to carry risks of viral infection e.g.; Hepatities B; HIV; Cytomegalo virus. Plasma is not freely available in all the hospitals and viscosity of adult plasma is higher than that of neonatal blood[6]. Normal saline is a readily available cheap substitute.

The present study was carried out to evaluate the efficacy and safety of normal saline versus plasma in correcting the hematocrit and symptomatology in polycythemic neonates.

Materials and Methods:

Over a period of one year; 26 newborn babies with symptomatic polycythemia were randomised to receive PEBT either with normal saline or plasma. Polycythemia was defined as a capillary hematocrit of greater than 70% and confirmed with venous hematocrit of greater than 65%.

500 neonates admitted to neonatal intensive care unit from Jan. 1998 to Dec. 1998 were screened for polycythemia immediately after admission and hematocrit was repeated later whenever indicated clinically. In symptomatic neonates, septicemia was excluded by a negative screen for sepsis and blood culture. Jitteriness was attributed to polycythemia when hypoglycemia, hypocalcemia, drug withdrawal and hypoxia were excluded. Respiratory distress in the absence of usual causes and normal chest roentgenogram was considered to be due to polycythemia. Babies who received blood transfusion were excluded from study.

Based on random allocation babies were subjected to PEBT either with normal saline or plasma. The aim was to reduce Hct to 55%. The amount of partial exchange done was calculated by the formula.

$$\text{Amount to be exchanged} = \frac{\text{Observed Hct - Desired Hct}}{\text{Observed Hct}} \times \text{Blood volume}$$

The blood volume was calculated as 85ml/kg. Before

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exchange and 6 and 24 hours after PEBT, venous Hct, electrolytes, coagulation profile (BT;CT; PT; PTT) and serum proteins were estimated. Symptoms of polycythemia were also looked for at 6 and 24 hours after PEBT.

The efficacy of treatment was judged by lowering of Hct and disappearance of symptoms. The safety of procedure was assured by change in heart rate; blood pressure and oxygen saturation.

Hct was measured with the help of REMI - 12C microcentrifuge at 14000 rmp for 3 minutes using heparinised capillary tubes.

Statistical analysis was done using students "t" test and a probability of less than 0.05 was considered to be statistically significant.

Results

Out of 26 symptomatic polycythemic neonates; 13 received PEBT with normal saline and 13 with plasma based on random allocation. Both the groups were comparable with respect to birth weight; gestational age and pre-exchange Hct.

There was a significant decrease in the mean Hct from 73.9% to 58.3% (P<0.001) at 6 hrs following PEBT in saline group and this change persisted at 59.5% after 24hrs (Table I). In the plasma group the mean Hct decreased from 73.7% to 58.4% (P<0.001) at 6hrs following PEBT and this change persisted at 59.7% after 24hrs. The change in Hct in the two groups was identical. In majority of infants, the symptoms disappeared within 24hrs of PEBT. However two babies in saline group and one in plasma group continued to be jittery at 24hrs. However they became symptom free within 48hrs of PEBT.

Serum electrolytes, coagulation profile and serum proteins remained normal and were comparable both pre and post exchange in the two groups.

Table-I: Change In Hct after PEBT

Group	pre-exchange 0hr.	6hr.	24hr.	pre-vs 6hr.	pre-vs 24hr.	6 vs 24 hr.
Saline group (n = 13)	73.9	58.3	59.5	<0.001	<0.001	NS
Plasma group (n = 13)	73.7	58.4	59.7	<0.001	<0.001	NS

NS = Not significant

Discussions

Increase in blood viscosity occurs linearly with rising Hct upto 65% but subsequently viscosity rises exponentially.

A high viscosity is associated with decreased tissue perfusion, oxygenation and multiple organ dysfunction[7]. PEBT in symptomatic polycythemia with normal saline or plasma ameliorates these symptoms and signs.

Plasma transfusion is associated with risks of transmission of serious viral infection. In addition the adult plasma has higher viscosity as compared to newborn blood, hence PEBT with plasma may lower Hct but Viscosity may remain unaltered.

Plasma may not be freely available everywhere as compared to saline. In the recent years normal saline has been shown to be a comparable alternative[8].

The present study showed a significant fall in Hct following PEBT which persisted even at 24hrs. in both saline and plasma groups. The drop in Hct in both the groups were comparable. Similar were the observations of others[8,9].

The symptoms of polycythemia disappeared in majority of babies following PEBT. However, two babies in saline group and one in plasma group continued to be jittery at 24hrs; after PEBT. Jitteriness in these babies subsided within 48hrs of PEBT. Similar were the observations of others[8]. No complications occured in babies undergoing PEBT through umblical venous route or peripheral route.

Conclusion

PEBT with normal saline is as effective and safe as PEBT with plasma; saline having the advantage of easy availability; low cost and no risk of transmission of infections.

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RADIOLOGICAL "NON-FUNCTIONING KIDNEY", EVALUATION BY TC-99M DTPA RENAL SCAN

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Abstract: Eighty patients of so called non-functioning kidney on excretory urography were studied by Tc-99m DTPA renal scan. 39(48.75%) of these patients showed significant renal function (split more than 20%) and thus could be salvaged by relevant surgical procedures. Tc-99m DTPA renal scan is mandatory before declaring a kidney totally non-functional.

Key Words: Non-functional Kidney, Tc-99m DTPA, Salvage, Split function, Renal scan.

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INTRODUCTION

Since the advent of radiological techniques excretory urography has been routinely used to ascertain the renal function. In the past all non-visualized kidneys were labelled as "Non-functioning" and invariably subjected to nephrectomy in order to avoid the associated complications. Availability of kidney specific radiopharmaceuticals and state of the art nuclear technology has made accurate quantification of renal function possible and helped to salvage a good number of the so called "non-functioning kidney".(1) Tc-99m DTPA (Technetium-99m Diethylenetriaminopenta-acetic acid) renal scan is reliable, noninvasive, without danger of allergic reactions associated with iodinated contrast agents and has no unpleasant side effects or excessive radiation dose to the organs involved.(2) Tc-99m DTPA renal scan provides information regarding the vascular perfusion, the split renal function, global and differential glomerular filtration rate (GFR) and thus helps salvage the kidney with a split renal function of more than 20%.(3)

Fig:I

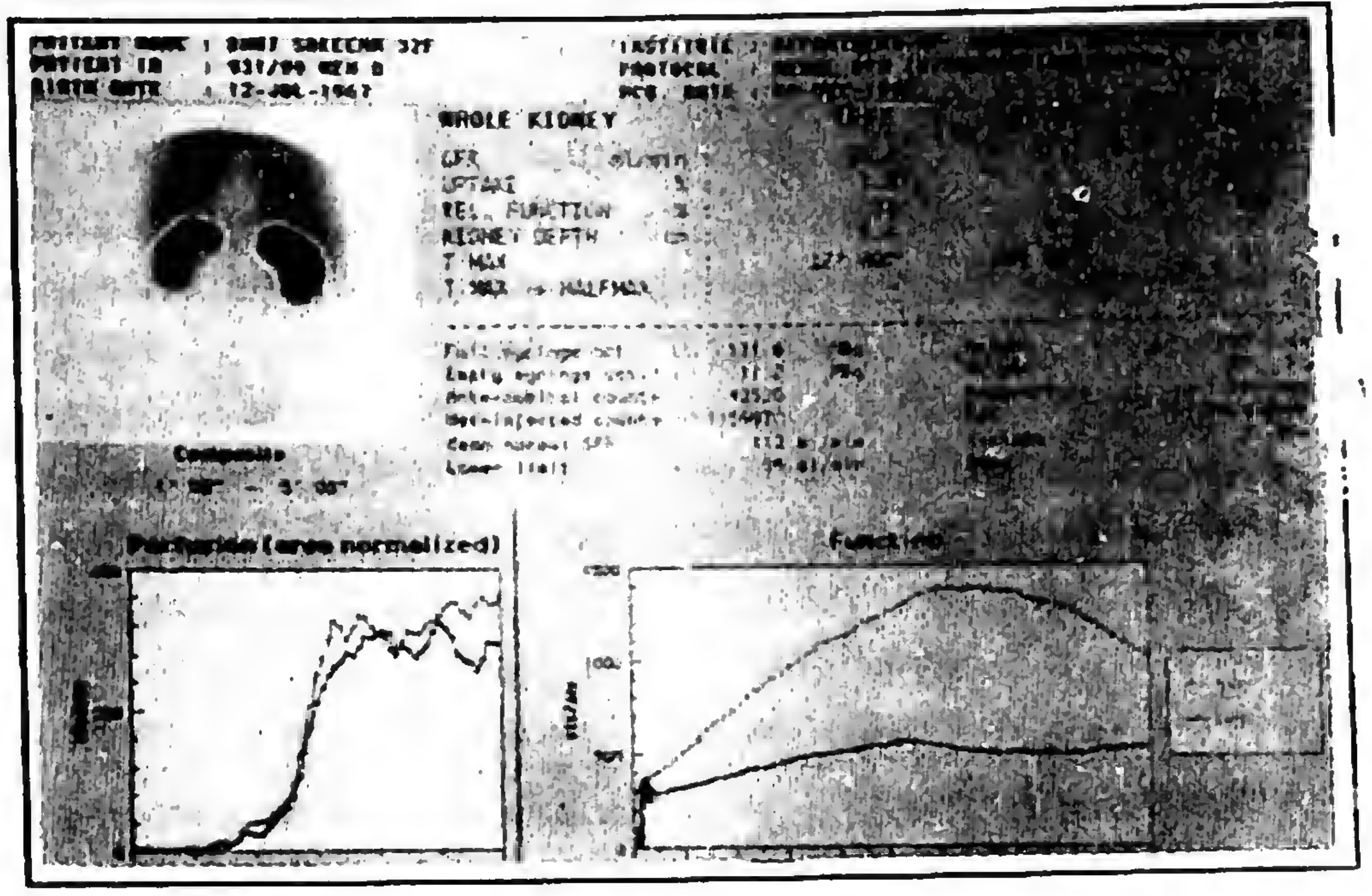

Fig:II

MATERIAL AND METHOD

After proper hydration 80 patients with the so called "Non-functioning Kidney" on excretory urography were studied by Tc-99m DTPA renal scan. After a bolus intravenous injection of 5-10 milli curies of Tc-99m DTPA rapid serial images of 1 second were acquired for 1 minute during the angiographic phase of the study. This was followed by acquisition of 30 seconds image for another 30 minutes. A pre-defined renal differential software programme was used to process the acquired data in order

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to calculate the split renal function and other related parameters.

RESULTS

A total of 80 patients (male=29, female=51) with radiologically documented "Non-functioning kidney" (left kidney=43, right kidney=37) were studied. 41(51.25%) patients had a split renal function of less than 20% and were confirmed to be non-functioning. In 36 patients the split function though reduced was still significant between 21-41%. 3 patients had a split function greater than 42% which is within normal limits of 50±8%.(4)

DISCUSSION

Generally kidneys work better than their radiological (excretory urography) assessment would suggest and too many kidneys contributing substantial renal function have been removed unnecessarily, particularly in the context of obstructive uropathy. In the present study of 80 patients with non-functioning kidney, 39(49%) patients had kidney's with a substantial significant renal function and thus could undergo surgical procedures to salvage them. Tc-99m DTPA renal scan should be an essential prerequisite before declaring a kidney non-functional and non-salvageable. As a matter of fact Tc-99m DTPA renal scan should be preferable over excretory urography because of its cost effectiveness, least side effects and quantification of renal function both before and after a surgical procedure.

Table 1: Tc-99m DTPA SPLIT RENAL FUNCTION IN 80 PATIENTS WITH RADIOLOGICALLY "NON-FUNCTIONAL KIDNEY".

SPLIT RENAL FUNCTION	NO.OF PATIENTS (%)	
NON FUNCTIONAL		
<20%	41(51.25%)	
FUNCTIONAL		
21-41%	36(45.00%)	} 48.75%
>42%	3(3.75%)	
TOTAL	80(100%)	

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CLINICO-BACTERIOLOGICAL PROFILE OF EMPYEMA THORACIS IN CHILDREN.

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***Abstract**: Empyema thoracis in children is very commonly seen all over the world, more frequently as a complication of pneumonic infections. An empyema is a purulent collection in the plural space. It constitutes an actual abscess and the pleurae formerly thin and glistening are now abscess walls, thickened granular & inflammed supporting pyogenic growth.*

Empyema was a frequent complication of pneumonia in childhood before the advent of antibiotics and its incidence dropped to almost negligible levels in the early period of antibiotic use, so the disease was considered to be extinct and over the last more than two decades the incidence has again increased and the commonest organism detected has been penicillinase producing staphylococcus. In this study fifty four patients (constituting 1.34% of total admissions) of empyema thoracis were encountered over a period of eight months, and the commonest age group involved was of 2-8 years. Majority of the cases were from rural areas and poor socioeconomic status with protein energy malnutrition of different grades. Nearly 60% patients had significant symptoms for more than one week at the time of presentation. Nearly 84% patients had received different combinations of antibiotics before admission in the hospital. Typical clinical features of effusion (splinting of chest, dull percussion note and decreased breath sounds) were seen in 62% to 88.88% patients. X-ray picture of effusion was present in all the 54 patients. Commonest organism isolated on culture was staphylococcus. The mainstay therapy was intercostal chest tube drainage and parentral antibiotics with cloxicillin as one of the antibiotics. Seven patients died due to the complications (e.g. septicemia, pericarditis and disseminated intravascular coagulation) and that too in the first few days after admission.

***Key words:** Empyema Thoracis, Antibiotic Sensitivety*

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Introduction

Since empyema thoracis is very common in our part of the country and the patients are encountered round the year and no such study has been conducted before, so it became mandatory to carry out one such study on the subject and bring the following facts to the surface.

1. Incidence of Empyema thoracis in paediatric admissions.
2. Mode of clinical presentation and complications of empyema thoracis.
3. Various aetiological agents involved.
4. Antibiotic sensitivity pattern.

Material and Methods

This study has been conducted in Govt. children hospital Srinagar between the months of October and May. During this period 54 patients of effusion were diagnosed clinically and radiologically, that were confirmed as empyema thoracis by thoracocentesis.

Detailed history of symptoms was taken including the symptoms and duration of symptoms, any associated Illness:, medicines used before the admission, social and family factors. Routine investigations i.e. hemogram, chest X-ray, Urine analysis were done and the fluid aspiration by pleural tap was subjected to cytological, biochemical and microbiological examination. Acid fast staining was done in all those cases, where tuberculosis was suspected. Pleural fluid culture and sensitivity was done in almost all the cases and the patient was empirically put on one of the antibiotic regimens (i.e cloxicillin + ampicilin, Cloxicllin+ crystalline penicillin, cloxicillin + gentamycin Cloxicillin + cefotaxime) and subsequently the antibiotics were changed according to the culture sensitivity report. While in the hospital the patients were monitored continuously by their clinical symptoms, signs and radiological findings. The intercostal drainage tube was put in to drain the purulent pleural fluid. As and where indicated the supportive treatment was given in the form of blood transfusion, oxygen therapy, intravenous fluids and nutritional rehabilitation. After discharge the patients were followed on outdoor basis and if indicated repeat

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X-ray films of chest were taken at 3 & 6 months after discharge or when the indication would arise.

Observations and Results

The study conducted revealed the incidence of empyema thoracis as 1.34% among the hospital admissions. Majority of the patients were in the age group of 2 to 6 years (Table-I) Males were 50% more commonly involved than females (Table-I). It was two times more common among rural population than in urban population (Table-I). More than 60% patients belonged to lower socioeconomic status group. Only 12.96% patients were from upper socioeconomic class. Only 33.33% patients had average weight while as 66.46% had protein energy malnutrition of various grades. (table-II) 50% patients had symptoms for one to two weeks before admission.

Table-I

Complaints	No. of cases	%age	age distribution				
			<1,	1-2,	2-5,	2-8,	>8
Fever	49	90.74	1	4	25	15	4
Cough	35	64.81	0	3	23	9	0
Breathlessness	34	62.96	2	5	18	7	2
Chest pain	17	31.48	0	1	10	5	0
Vomiting	13	24.07	1	3	5	3	1
Measles rash	5	9.25	0	1	4	0	0
Anorexia	44	81.48	2	5	22	13	2
Whooping cough	3	5.55	0	1	2	0	0
Cyanosis	9	16.66	2	2	5	0	0

Statistical table showing symptom distribution of the patients.

83.33% patients had received various antibiotic combinations before admission. Most significant symptoms and signs at the time of admission were in the form of fever, cough, breathlessness, chest pain, vomiting, Anorexia, Paroxysmal cough (table-III), Tachycardia, Tachypnoea, dyspnoea, Pallor, dull percussion note & decreased breath sounds (table-IV). Radiological evidence of right sided effusion was present in 50%, effusion was left sided in 42.5% and bilateral in 7.40% patient. Pneumothorax was present in 20.37% & pneumatoceles in 27.77% patients (Table-V).

Investigations revealed anemia as a very common association in the patients of empyema thoracis. Hemoglobin less than 8 gm/dl. was in nearly 1/3d (35%) patients, and 8-10gm/dl. in 46% patients. 55.31% patients had positive culture, out of which majority had staphylococcal growth. Culture of 44.69% patients did not reveal any growth (table-VI)

Antibiotics were used according to the culture sensitivity results. Majority of the patients responded to cloxicillin used in combination with various other antibiotics (i.e crystalline penicillin, ampicillin, gentamycin, cefotaxime) Ampicillin and gentamycin without cloxicillin were used in two patients. Two patients were treated with antitubercular treatment in addition to antipyogenic therapy. Average hospital stay was 10-21 days, two patients were discharged after 30 days and one patient after 39 days who developed generalized sepsis. Intercostal tube drainage was done in all patients. Three patients needed decortication. Out of 54 patients 7 patients died that also during the first few days of admission, Deaths occurred more commonly in the young age group and in the patients who had associated malnutrition and Anemia.

Table-II

Clinical picture	No. of cases	%age	Age distribution				
			<1,	1-2,	2-5,	5-8,	>8
Tachycardia	51	94.44	2	5	27	14	3
Tachypnoea & Dyspnoea	49	90.74	2	5	24	15	3
Grunting	15	27.77	2	3	6	2	2
Splinting of chest	34	62.96	0	0	19	12	3
Dullness to P/N	45	83.33	1	3	24	14	3
Decreased breath Sounds	48	88.88	2	3	25	15	3
Abdominal Distention	7	12.96	2	2	3	0	0
Dehydration	16	29.62	1	3	7	4	1
Pallor	40	74.07	2	4	20	11	3

Statistical table showing clinical features.

Discussion

Incidence of empyema thoracis seen in this study is higher than reported in some other studies e.g. 0.11% by Khan A.A. etal (1978), 0.87% by Karmakar D.P. et al (1978) 0.11% by Arya L.S et al (1982), so the higher incidence found in this study appears to be due to the several factors, most important of which is the cold climatic condition in the valley of Kashmir, due to which the respiratory tract infections and its complications are more common as is evidenced by the empyema thoracis being seen more frequently during winter months, other factors include the poor nutrition and delayed and inadequate access to the medical facilities. Age group involved more commonly is 2-6 years, with little predominance in males as is supported by earlier studies also e.g Lata Kumar et al (1980). Padmini, R et al (1990) . The disease is very common in poor socioeconomic class and the protein energy malnutrition is seen as a very common association of empyema thoracis.

Table-III

Radiological Findings	No. of cases	%age of case
Right sided effusion	27	50.00%
Left sided Effusion	23	42.49%
Bilateral Effusion	4	7.40%
Pneumothorax present	11	20.37%
Pneumatoceles present	15	27.77%

Table showing radiological features.

Patients of empyema thoracis usually have the preceeding illness in the form of upper respiratory tract infection, pneumonia, pertussis, measles, otitis media, etc. Acute onset empyema thoracis is rare.

Table-IV

Organism grown	No. of Patients	%age
Staphylococcus	17	36.17%
Pneumococcus	4	8.48%
Pseudomonas	3	6.38%
Streptococcus	2	4.25%
No growth	30	63.82%

(Total bacteriological cultures drone= 47)

Table showing bacteriological culture results.

Out of 47 cultures 26 were positive out of which 17 (65.38%) showed staphylococcal growth. Other organisms recovered were pneumococcus, pseudomonas & streptococcus. Reason for the nega- tive culture was prior antibiotic therapy which was given in 83.37% patients in this study. Similar bacteriological studies have been shown in other studies e.g Lata Kumar et al (1980) has shown 24 staphylococcal growths out of 44 postive cultures, and Arya L.S et al (1982) reported 17 staphylococcal growths out of 27 positive cultures.

It has been seen that in vitro antibiotic sensitivity does not correspond with the in vivo antibiotic sensitivity in all the cases.

Cloxicillin is the drug of choice in combination with one or more of the other antibiotics e.g Crystalline penicillin, gentamycin, ampicillin or a third generation cephalsporin depending upon the individual response. Because of the indiscriminate use of the antibiotics in our set up, the prior antibiotic therapy is received by all the patients before they are actually diagnosed as having empyema thoracis and admitted in the hospital and it makes the isolation of organism a difficult task. Intercostal tube drainage with antibiotic therapy is the mainstay of treatment in empyema thoracis, apart from that care is to be taken of nutrition, anemia and other associated problems, and essential supportive care is to be rendered.

In the present study the observed mortality rate of 12.96% is not significantly different from what has been observed in other earlier studies. Deaths due to empyema thoracis are more common in the younger age group (less than 2 years) as has been reported by Narayanan I.K et al (1972), especially when protein energy malnutrition is present. So the young age and protein energy malnutrition constitute the most important bad prognostic factors in childhood empyema thoracis. Sterile pleural fluid as demonstrated by culture has no bearing on the prognosis. Dissemination of the infection and multisystem involvement are the important factors leading to higher mortality.

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HEARING LOSS – A RARE POST LUMBAR PUNCTURE COMPLICATION TREATED BY EPIDURAL BLOOD PATCH.

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***Abstract:** We report a case of acute onset of hearing loss after lumbar puncture for aspiration of C.S.F., treated by an epidural blood patch. After review of literature we found that his is only the second case of Post Lumbar Puncture hearing loss treated by epidural blood patch.*

***Key words:** Lumbar puncture, Hearing loss, epidural blood patch.*

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Introduction

Lumbar puncture for myelography, spinal anesthesia and aspiration of cerebronpinal fluid (C.S.F) is a very common procedure. Complications of lumbar punture (LP) like headache, dizziness, and even complications involving cranial nerves, eg, oculomotor, trochlear, abducens, and facial nerve, are well recognized. But hearing loss as a sequelae of lumbar puncture has rarely been reported, although the first publication about this complication dates back to 1914.

Case Report

A 45 year old physician was hospitalized for headache since past 48 hours photophobia, neck pain and fever. On admission patient had nasal herpes zoster complicated by M.R.S.A. (Methicilline resistant Staphylococcus Aureus) cellulitis. Patients lab's were normal except for neutropenia secondary to trimethoprim sulphametha oxazole which the patient was taking prior to being hospitalized. A computed tomography (C.T.) of the head done on admission was normal. Lumbar puncture was performed on day of admission, using a 20 gauge L.P. needle. C.S.F. analysis and culture were normal. After half an hour of performing L. P. patient complained of severe postural headache, dizziness, diaphoresis (when upright), and complete loss of hearing in his left ear. A bed side hearing test disclosed complete hearing loss on the left side. Patients headache and hearing loss did not improve despite conservative measures such as bed rest, fluid intake, and I.V. infusion of caffeine. On day 4 of admission an epidural blood patch was performed. Autologous blood (20 ml) was injected into the epidural space at the site above the previous lumbar puncture site. Within half an hour of performing the blood patch both the patients hearing and postural headache showed remarkable improvement. The pure tone audiogram done a week later documented a left sided, high frequency hearing loss. A repeat audiogram done after a month showed improvement of 10 db in high frequency hearing on left side with some residual hearing loss in high frequency tone.

Discussion

Post lumbar puncture hearing loss may occur with or without accompanying postural headache. Minor hearing loss after L.P. may occur more often than postural headache[7]. Vandham and associates demonstrated that with a few exceptions hearing troubles were associated with typical postural headache[2]. In some studies hearing loss after L.P. varied from 8% to 42%. This led Viale and associates to suggest that postural headache may mask Post Lumbar puncture auditive symptoms[6]. The severity of hearing loss is always associated with severity of headache. Significant hearing loss is always accompanied by headache[5,7]. Hearing loss following Lumbar puncture is either unilateral or bilateral. In almost all cases it is limited to low frequency tone range[7,8,5,13]. Though our patient had hearing loss in high frequency tone. In majority of cases hearing loss and other neurological sequelae occur within 48hrs of L.P.

The hearing loss following L.P. is attributed to mechanical disturbance due to low intracranial pressure secondary to leakage of C.S.F. through dural puncture[2,5,13,14]. It is postulated that decreased C.S.F. pressure results in caudal displacement of brain leading to traction and ischaemic stretch to pain sensitive intracranial structures. Some authors are of the view that hearing loss post lumbar puncture occurs usually in patients with an open or only partly closed cochlear aqueduct. As there exists an anatomical link between cochlea and the subarachnoid space, via the cochlear canal and also the composition of perilymph in the

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perilymphatic fluid closely resembles the cerebrospinal fluid. It is assumed that the loss of C.S.F. during or after L.P. results in a loss of perilymphatic fluid. The resultant lowered perilymphatic pressure in relation to endolymphatic pressure leads to an endolymphatic hydrops and displacement of the bsement membrane. This may explain the fact that hearing loss is mostly, reversible[4]. The individual risk of post-spinal puncture hearing loss cannot be predicted as even high-resolution computed tomography cannot delineate the aqueduct and its internal soft tissue anatomy.

Hearing loss occuring post L.P. is also related to size of needle used. Rate of C.S.F. leakage may vary form 0.47 ml/mm to 11-9 ml/mm depending on needle size[15]. Usually, recovery from hearing loss and other complications follows bed rest, fluid intake, intravenous infusions, psychological reassurance. In patients who fail to respond to conservative measures, epidural blood patch can be performed[3]. The epidural blood patch technique has been in use since 1960[15,16]. This method has proved to be safe and effective for treating post lumbar puncture headaches and hearing loss[17,3]. Complications reported with epidural blood patch included back pain, neckache and slight elevation of temperature. Rarely, meningeal irritation has also been reported[18,19]. Though most reported cases of Post lumbar puncture hearing loss are reversible, but permanent hearing loss post lumbar puncture has also been reported[4,20].

Conclusion

Hearing loss post L.P. can be divided into 2 categories. a) Hearing loss with headache, b) Hearing loss without headache. Hearing loss usually occurs in low frequencies but it can occur in high frequencies also, though very rarely, as documented in our case. It can be unilateral or bilateral. Hearing loss and headache can be reduced by use of proper technique and use of small sized needle for L.P.

The epidural patch can be used as an effective means of treatment in patients who fail to respond to conservative measures.

As post L.P. hearing loss occurs much more commonly than reported, physicians should be aware of this complication, and should inform patients about this complication for medico legal reasons.

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CUTANEOUS METASTASIS FROM ESOPHAGEAL SQUAMOUS CELL CARCINOMA IN A PATIENT OF ACHALASIA - A RARE ENTITY

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Abstract: We describe a patient of long standing achalasia who subsequently developed squamous cell carcinoma esophagus and presented with a cutaneous metastasis.

Key words: Achalasia, Squamous Cell Carcinoma, Esophagus.

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Case Report

70 year old patient was labelled as achalasia cardia on the basis of Barium esophagogram which was done on him at a local place for intermitent dysphagia in his childhood. Due to non availability of other diagnostic modalities i.e. esophagogastro-duodenoscopy and esophageal motility studies, patient was left alone to face the intermittent dysphagic complaints with some dietary intake advice. About a month back patient presented to our department with worsening of dysphagia and a hard swelling was observed by him in the neck region. In the recent past he also experienced weight loss and generalised weakness. On physical examination patient was dehydrated, emaciated with mild pallor. Chest, cardiovascular and abdominal examination revealed no abnormal findings. There was a 4 x 3 cms rounded stony hard, non mobile and non-tender swelling in the region of manubrium sterni.

Except for mild anaemia (Hb = 9.5 gms/dl) haematological parameters were normal. Kidney and liver function tests were also normal. Esophagogram revealed grossly dilated esophagus with beaking at its lower end. There was a 7cm long stricture at the level of D_7 vertebra. Endoscopy revealed ulcero-infiltrative lesion from 25-32 cms. Below the growth, esophageal cavity was filled with dirty foul smelling food material and resistance was felt at gastroesophageal junction. Stomach and duodenum were normal at endoscopy. Biopsy of the lesion revealed well differentiated squamous cell carcinoma. Fine needle aspiration of the swelling at manubrium sterni revealed metastatic deposits from squamous cell carcinoma. Esophageal manometric studies were not done due to technical problems in inserting the catheters through the malignant stricture. Patient was managed with endoscopic pneumatic dilatation for Achalasia cardia. For malignant stricture of exophagus patient was followed up on a two weekly dilatation protocol by savery gillard esophageal dilators. Due to poor ECOG status and considering the stage of the disease patient was declined to receive any other form of treatment by the department of radiation oncology.

Introduction

Achalasia is known to be a predisposing factor for the developmen of esophageal cancer[1], however, subsequent development of metastatic lesions in the skin is not reported till date to the best of our knoowledge. We herein report a patient with long standing Achalasia presenting with a neck swelling and worsening of dysphagia. Diagnosis of malignancy was achieved from the esophageal biopsy and fine needle aspiration cytology of the neck swelling. Though esophageal monometry was not performed,barium esophagogram, endoscopic examination of the gastroesophageal junction, clinical improvement with the pneumatic dilatation and above all the long standing clinical symptoms in this patient were reassuring to the diagnosis of Achalasia cardia.

Discussion

Achalasia a benign disease is compatible with long life but the complications like development of malignancy often occuring late in the illness may result in morbidity and mortality. The risk of developing malignancy in achlasia is 2.9%[1,2]. Esophageal squamous cell carcinoma spreads chiefly by direct extension and occasionaly by way of lymphatics and blood. Although metastasis from esophageal squamous cell carcinoma can at times have a wide distribution, cutaneous metastasis is unknown. Skin metastase may indicate progression of the tumour and early fatal termination.[3] Our patient was unique, as he had cutaneous metastasis in the absence of extra-cutaneous metastasis. This supports the hypothesis of

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organ specific metastasis purposed by Paget[4] and suggests the presence of a clonal population of carcinoma cells with a high cutaneoous affinity and a low affinity for other organ systems[5].

We suggest periodic endoscopic examination of esophagus in patients with long standing Achalasia to rule out any development of malignancy. A thorough physical examination to look for cutaneous nodules should not be ignored.

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LEIOMYOSARCOMA - A CASE REPORT

Shahida Mir M.D.; Nighat Firdous M.D.; A. R. Khan MD.

Abstract: *A case of leiomyosarcoma occuring at a very young age is reported here. This patient had undergone "Lapratomy" for a pelvic mass consequent upon the diagnosis of Leiomyosarcoma in histopathological examination. Total abdominal hysterectomy with bilateral salpingo oophorectomy was performed. Later the patient received six cycles of chemotherapy. The patient was followed for eight months and was disease free.*

Key words: *Leiomyosarcoma, Total abdominal hysterectomy, Bilateral salpingo oophorectomy.*

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Introduction:

Sarcoma of the Uterus, a mesodermal tumour accounts of only one percent of female genital tumours, yet it is the most malignant of all the uterine tumours. It can occur in a variety of forms but the three most common variaties are leiomyosarcoma, endometrial stromal sarcoma and malignant mullerian mixed tumour[1]. Sarcoma in a leiuyoma is the most frequent form of sarcoma of Uterus[2]. The risk of Sarcomatous change in a fibroid has been variously quoted as ranging from 1 to 8 per 1,000. The tumour is difficult to differentiate from benign cellular leiomyoma.

Case History:

A 26 year old un-married female presented to the Hospital with complaints of pain in the lower abdomen and vomiting. Her menstrual history and general physical examination was unremarkable. On palpation a swelling of 28 weeks uterus size was found arising from the pelvis. Ultrasonography revealed at 21.6 X 14.3 cm cystic mass arising out of the pelvis with multiple septation. No internal echoes were seen. Its relation to either ovary could not be made out. Back pressure changes were seen in both Kidneys. The swelling was reported as "Ovarian Cyst". The patient under went Lapratomy where a huge Cystic Swelling arising within the uterus was present. The swelling involved the whole uterus, compressing the myometrium to a thin layer. The swelling was dissected and redundant portion of uterus was trimmed. the uterus was then closed back. Both tubes and ovaries were healthy.

Pathology:

On gross examination the tumour appeared grey yellow, soft with frequent regions of necrosis and haemmorhage.

Fig. I

Microscopic Appearance:

On histopathalogy, growth was reported as "leiomyosarcoma" of moderate grade. Highly cellular areas consisting of oval to round cells were seen. Cells showed moderate pleomorphism. Mitotic count was >10/10 HPF. The metastatic work up of the patient was negative. later Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. No residual disease was found in the uterus and the ovaries. The patient received six cycles of chemotherapy with cyclophosphamide, adriamycin and cisplatin.

Discussion:

The first tumour described as a Uterine Sarcoma was presented before a meeting of Berlin Obstetric Society by May 1859. The median age at presentation varies from 43 to 56 years in different series.

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Leonard A. Aaroetal (1959) reported that the ages of the patients at the time of diagnosis of "Leiomyosarcoma" ranged from 69-74 years with an average of 50.2 years[3]. Our patient was 26 years old.

"Leiomyosarcoma" are rapidly progressive tumours. They are characterised by a pattern of wide spread metatasasis which leads to early death[4]. Surgical exploration for adequate staging should be done and if resectable total abdominal hysterectomy with bilateral Salpingo-Oophrectomy should be performed. If the patient is not fit for surgery then Radiotherapy should be given with curative intent. Chemotherapyor prophylactic irradiation may be given to upper abdomen and lungs to decrease distant metastasis[5].

Five year survival rates of 20-63% have been quoted. Mitotic counts and extent of disease at the time of lapratomy are the prognostic indicators. Both Gudgeon (1968) and Silverberg (1971) have reported a better prognosis for premenopausal patients[6]. Uterine sarcoma are rare tumours. Nevertheless the tumors represent the most intriguing and perhaps the most malignant of all tumors. The poor prognosis associated with these tumors, the scanty reports in the literature with conflicting opinions regarding their management have posed a real therapeutic challenging for the gynaecologists.

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BILATERAL UTERINE ARTERY LIGATION FOR CONTROL OF OBSTETRIC HAEMORRHAGE AND AN ALTERNATIVE TO HYSTERECTOMY

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Abstract: *Postpartum hemorrhage occurring after vaginal delivery or caeserian section is a known complication of parturient and poses a challenge to save the uterus. For this bilateral uterine artery ligation was successful and simple technique carried out in 22 patients.*

Key words: *Post partum hemorrhage, Uterine artery ligation.*

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Introduction:

One of the leading causes of maternal morbidity and mortality still continues to be obstetric hemorrhage. It results mostly from uterine atony or placental pathology. The control of such an emergency is brought about by conservative methods. But sometimes these procedures fail and emergency hysterectomy has to be employed.

In view of an increasing incidence of emergency caeserian hysterectomy and puerperal hysterectomy in the management of postpartum haemorrhage, emphasis should be placed on safe routine methods to identify and ligate the uterine vessels when indicated[1]. Bilateral internal iliac artery ligation has been done to control PPH with great success along with the saving of uterus[2]. Uterine artery is a branch of internal iliac artery. During pregnancy 90% of blood supply to uterus comes from the uterine arteries with minimal blood flow from the ovarian cervical and vaginal vessels. Thus a significant hemostasis can be achieved by bilateral uterine artery ligation. The blockage of uterine blood supply is a temporary procedure, recanalisation is almost a rule and normal uterine circulation is established in due course of time, thus preserving various uterine functions like menstruation and pregnancy.

Method:

The uterus is grasped and elevated with the left hand, a large Mayo needle with a No. 1 atraumatic chromic catgut suture is employed to ligate the left uterine artery,the needle is passed into and through the myometrium, from anterior to posterior 2to 3 cms. medial to the uterine vessels then brought forward through the avascular area of the broad ligament lateral to the artery secured.

The right uterine artery is then ligated, the needle being passed from anterior to posterior through the avascular area of the broad ligament and brought anteriorly through the myometrium 2 to 3 cms. medial to the artery and vein. Following ligation the musculature assumes a pinkish hue secondary to the ischaemia and increased tone may result. It is not necessary to mobilise the bladder as the sutures are not placed that low, and there is no fear of ureteral damage since they enter the bladder trigone well below the ligature site. Since the ligation will usually be done during the course of a caeserian section, the suture is placed below the level of the transverse uterine incision beneath the reflected flap of peritonium.

The vessels are not divided thus only a single ligature is performed on each side.

Observation and Discussion:

The study was conducted on 22 patients from January, 1988 to June 1999. Table I shows the various indication for bilateral uterine artery ligation.

Table-I: Indication of bilateral uterine artery ligation:

S.No.	Indication	No. of patients	%age
1.	Atony	13	59.0
2.	Placenta Previa	4	18.0
3.	Abruptio placentae	2	9.0
4.	Couvelair uterus	2	9.0
5.	Placenta Accereta	1	5.0
	Total	22	100.0

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Table-II: Indication for uterine artery ligation in relation to age, parity:

S. No.	Indication	Mean age	Parity Primi	Parity Multi
1.	Atony (n=13)	27	9	4
2.	Placenta previa (n=2)	24	2	2
3.	Abruptio placentae (n=2)	26	1	1
4.	Courvlair uterus (n=2)	29	0	2
5.	Placenta accreta (n=1)	28	0	1

The mode of delivery in all the patients was lower segment caeserian section, and the fetal outcome was that 21 live babies were delivered. There was one still birth in a patient who had concealed accidental haemorrhage.

The age of the patients ranged from 23 to 34 years and the mean age of the patients for different indications were comparable. 12 patients were primigravida and 10 were multi-gravida. Out of 22 patients, bilateral uterine artery ligation was effective in controlling PPH in 21 cases. In one case who had placenta accreta, bilateral uterine artery ligation was followed by subtotal hysterectomy. This had to be done to save the life of the patient. Fahmy[3], Oleary et al[1], Druzen[4] have also noted failure to control PPH in cases of placenta accreta. Abdrabbo[5] also reported the inability to control the PPH in 4 cases (2 placenta previa and 2 accreta). But he was able to save the uterus by ligation of uterine vessels very low 3-5 cms. below the upper ligature after its cervico-vaginal branch has turned abruptly upward to extend along uterus margins.

In 21 cases, the procedure was fully effective. Fahmy[3], Abdrabbo[5], Noor Afshan[6] have also found that bilateral uterine artery ligation was 100% effective in all except those cases of placenta previa and accreta where failure rate ranged from 8 to 20%. In the present study, the mortality from this procedure is nil which has also been observed by other authors[6]. Oleary et al[1] have reported 2 cases of broad ligament haematoma which can be easily avoided by choosing avascular area in the braod ligament. This complication has not been observed in our study. Other complications like arterio-venous fistula,uterine necrosis or uterine injury have not been seen in our series of patients. 2 of our patients had bicornuate uterus and both underwent successful bilateral uterine artery ligation.

The patients are being followed up regularly and menstruation has started in 15 of the 22 patients. The patients are doing well.

Conclusion:

Uterine arteries are extremly easy to identify and ligate. The procedure is safe and excellent for management of PPH, where all the methods have failed. Excluding the case of placenta accreta, this procedure was cent percent effective. Hence we must always choose this procedure whenever indicated. It also ensures the preservation of the uterus which otherwise leaves a severe physical and psychological trauma for the young patients.

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DISRUPTION OF PATCH AORTOPLASTY BY SALMONELL TYPHAE

A.G. Ahangar M.S., M.Ch.; A. Majeed M.S., M.Ch.;.; I.A.Mir M.S.; N.A. Lone M.D.

Abstract: *Coarction of postductal aorta was repaired by a dacron patch in a 14 year old boy. It got infected by salmonella paratyphae and patient died inspite of receiving the treatment for salmonella infection.*

Key words: *Patch Aortoplasty, Salmonella Infection*

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A 14 year old boy was admitted in department of CVTS (SKIMS) Srinagar Kashmir with the complaints or pain left side of chest and abdomen,vomitting and high grade fever associated with rigors and chills.

The patient had undergone patch aortoplasty (Dacron) for coarctation of aorta around 40 days before with uneventful per-and postoperative period and was discharged on 10th. post operative day. The examination of the patient revealed temp. of 102 F, severe anemia, tachycardia, hypotention and hepatosplenomegaly. The patient was put on injectable Ciprofloxin and Gentamycin after taking the blood for complete naematological examination, kidney function tests, electrolytes, liver function tests, ASO/CRP, widal test and blood culture for culture sensitivity.

Investigative profile revealed HB of 6gms/dl., total leukocyte count of 22000/cmm (Neutophils 89%) plat. 80,000/ cmm PTI of 70% and total serum proteins 5 gms/ dl, blood cultures grew nonlactose fermenter salmonella typhae (sensitive to Ciprofloxaxacin Amikacin) and mediastinal widening in X-ray chest. Echocardiography was normal. The treatment was continued with Inj, Ciprofloxacin, Amikacin and in addition patient was transfused two units of fresh blood. The patient was on treatment for 4 days with little improvement in fever, tachycardia and anemia. Repeated blood cultures done on 2nd and 3rd day of admission were sterile. On 4th day of admission patient suddenly complained of severe pain on left side of chest with examination revealing severe pallor, perspiration, laboured breathing with unrecordable pulse, blood pressure and clinical evidence of effusion on left side with thorcocentesis revealing haemothoorax and blood was comming freely. The patient died after 30 minutes trial of resuscitation. The autopsy done revealed lot of blood in left side of chest with disruption of the upper part of the patch. A segment of patch, aorta and blood was taken for culture sensitivity. All the three showed growth of salmonella typhae. Diagnosis of patch disruption following infection of patch and suture line by salmonella typhae was made.

Discussion

Prosthetic graft infection is life threatening and every effort should be made to prevent it's occurrence[1,2]. Meticulous surgical technique, strict attention to operating room asepsis and perioperative antipiotic therapy have all helped to reduce the incidence to less than 2 percent. Despite this, late complications of prosthetic graft may occur during periods of bacteraemia[3]. Bacteraemic seeding presumably was the mechanism in this case.

Infection of the aortic grats with enterobacter aeroginosa has been a rare event[4,5]. The organism of the present case being sensitive to ciprofloxacin and amikacin did not respond. It is belived that the infection by the organism had caused extensive sloughing over suture line and ultimately disruption[6]. Russel A.J. et al (1992) reported salmonella infection of a dacron aortic bifurcation graft, local graft excision with extraanatomic bypass resulted in a successful outcome in their case[7]. In time exploration wound have saved the patient although with an increased risk.

We hereby conclude that if infection of a graft is suspected and the patient is not responding to antibiotics, immediate surgery with excision of the infected graft replacing it with a fresh one should be peformed.

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CHEST WALL RECONSTRUCTION - AN INDIGENOUS TECHNIQUE

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Abstract: *Reconstruction of the chest wall defects following tumor excision requires prosthetic materials for correcting skletal instability and myocutaneous flaps to provide soft tissue cover. Prolene mesh and goretex soft tissue patch arepresently preferred prosthetic materials for chest wall reconstruction. We present an indigenous technique of silver plate implantation for skeletal reconstruction of chest wall defects. Silver plate is locally available, easy to sterilize and handle, and is cost effective.*

Key words: *Chest wall, Tumor, Reconstruction, Prosthetic Material, Silver Plate.*

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Introduction

Chest wall tumors encompass a kaleidoscopic panorama of bone and soft tissue disease. Most patient as painful, enlarginng masses and may be tumors that have recurred or persisted following previous resection or irradiation. Surgical extirpation is frequently the only definitive method of treatment and this may be compromised by incorrect diagnosis or an inability to reconstruct the large chest wall defects. It represents a major challenge and requires close cooperation between cardiothoracic and reconstructive surgeon to achieve an optimal outcome and reduce the incidence of coomplications[1].

Advances in chest wall reconstruction utilizing autogenous tissue or prosthetic material has resulted in more aggressive resection of these tumors[2]. Stabilization of skeletal framework of thorax is accomplished best with prosthetic material prior to soft tissue reconstruction with or without coverage with musculocutaneous flaps or the omentum[1-8].

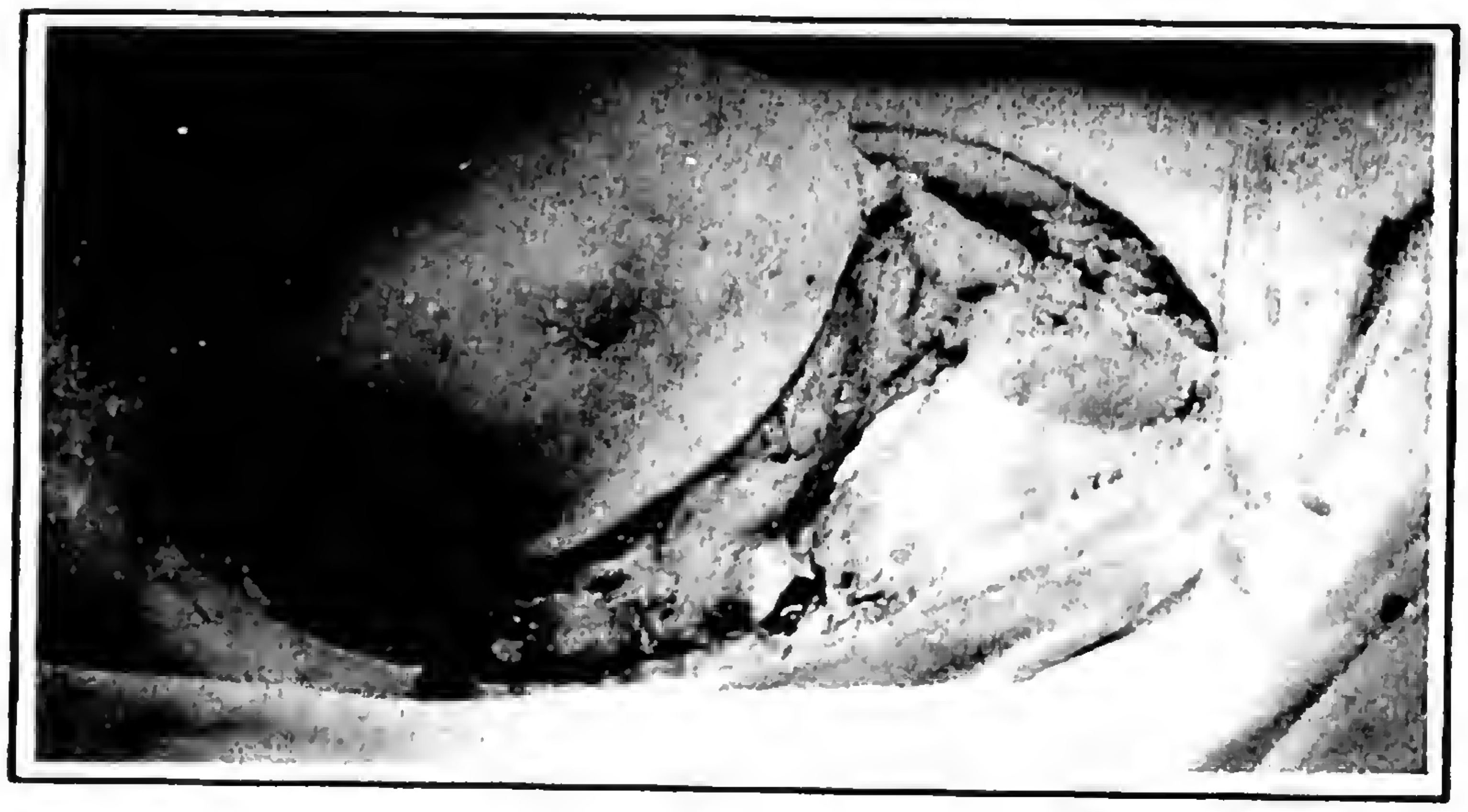

Fig. I:

We present an indigenous method of chest wall reconstruction using a silver plate, which is easily available, ways to handle and sterilize, and is cost-effective.

Technique of reconstruction

Silver plate, 0.5mm to 1 mm thick is prepared from a silver bar of good quality. It is maleable and required size can be easily cut with heavy scissors. The plate is sterilized in an autoclave. En-block-excision of the chest wall tumor is performed with adequte resection margins (4cms in a malignant neoplasm). After assessing the size of the chest wall defect, the silver plate is cut to required size with heavy scissors. With a fine drill small holes are made in the ends of resected ribs and at the corresponding sites in the plate, 1 cm away from margins. Superiorly and inferiorly small drill holes are made in the shafts of the unresected ribs and in the silver plate at the corresponding sites. Stainless steel wires No. 5 or 6 are passed through the drill holes in the ribs and silver plate. The wires are tightened, twisted and excess wire cut off; as if done in the closure of the midsternotomy. This provides a stable anatomical contour to the chest wall. The procedure may be combined with transfer of autogenous muscle or myocutaneous flap, to provide soft tissue cover for the reconstructed chest wall defect.

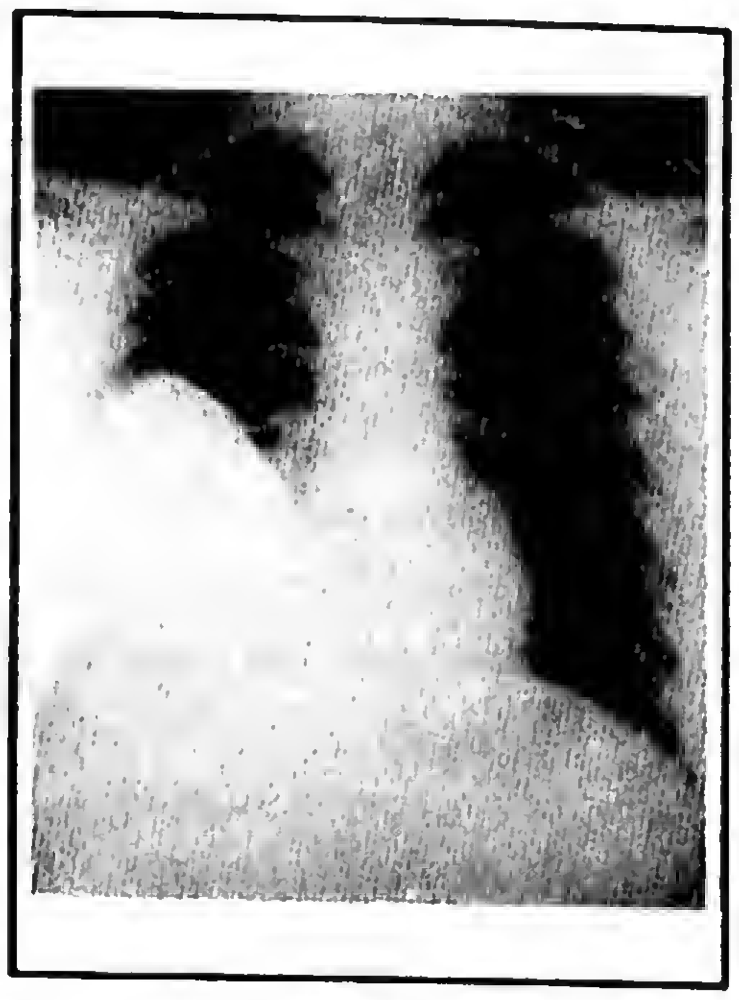

Fig.II:

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Case report

A 32 year old male, presented with a painful chest wall swelling just below the right breast (lower outer quadrant). The nipple was lifted up by the swelling. The mass was fixed to the chest wall. Fine needle aspirtion cytology revealed the diagnosis of epithelial cell sarcoma. Patient was taken up for excisional bipsy of the tumour. The tumor was engulfing 4th and 5th ribs from mid clavicular to mid axillary line and was invading middle lobe of the lung. En-block resection of the tumor with a resection margin of 4 cms along with 3rd, 4th, 5th amd 6th ribs was performed (Fig.I). A middle lobectomy was also performed to ascertain adequate clearance of the tumor. The resultant chest wall defect measuring 10x8cms was reconstructed using a silver plate as described above. Two chest tube drains were placed in the thoracic cavity. The reconstructed chest wall area was covered with locally mobilised myocutaneous flap (pictoralis major). Chest drains were removed on second postoperative day. Patient was discharged on 10th postoperative day. Histopathological examination of the excised specimen confirmed the diagnosis of peripheral neurileimoma. Patient did not have any complications due to silver plate till date (10 months follow up) (Fig. 2).

Discussion

Chest wall tumor is a generic term that includes primary neoplasm (both benign and malignant) of the bony skeleton; chest wall metastases, neoplasms that invade the chest wall from lung, pleura, mediastinum, muscle and breast. Wide resection of the chest wall tumor is essential to successful management[3]. Howerver, the extent of the resection should not be compromised because oof an inability to close the chest wall defect[2,4]. All primary malignant neoplasms should be excised en-block to include all of the involved bone and a 4cm margin of normal tissue[5].

Large full thickness chest wall defects might produce skeletal instability that should be taken into consideration along with the individual patient's pulmonary reserves and managed simultaneously with soft tissue reconstruction[1,6,7,11]. Defects upto two ribs can be reconstructed with muscle flaps only and will maintain good stability of the chest wall[2]. Large defects in the interior and lateral chest wall require re-establishment of the skeletal continuity prior to soft tissue reconstruction, particularly in patients with limited pulmonary reserves[1,6,7]. Most surgeons favour the use of prolene mesh or polytetrafluoroethylene (PTFE, Gore-Tex) 2mm soft tissue patch to re-establish the continuity and stability of the bony thorax[2,9,10]. Others have used autogenous rib grafts[4], Marlex mesh[8] or methyl-methaacrylate impregnated meshes[9]. The difference between prolene and Marlex mesh is that prolene is double stitch knit whereas Marlex is single stitch knit. Prolene is rigid in all directions, whereas Marlex is rigid in only one direction[2]. The main advantage of the Goretex patch over the synthetic or absorbable meshes is that it provides a complete separation of thoracic cavity from the overlying soft tissues[1].

Synthetic meshes (prolene, marlex), gore-tex soft tissue patches, and methyl-methacrylate impregnated meshes are imported and are too costly for an average Indian patient. Silver plate is available locally, sterilized by autoclave, maleable, can be cut easily with heavy scissors, and is easy to handle. Besides the cost of the metal is affordable for an Indian patient. It also has the advantage of separating the thoracic cavity from the overlying soft tissue. It is impermeable to water and air so the fluids from chest cavity are prevented from leaking under the soft tissues or muscle flaps. Besides it acts as a barrier (similar to Gore-Tex), preventing the tumor spread into the chest cavity in cases of recurrences[2]. It is meleable but rigid enough to provide stability to the skeletal frame work of thorax.

Comment

Reconstruction of chest wall defects using silver plate is a feasible alternative to the available prosthetic materials. It should be utilised wherever the imported prosthetic material cannot be afforded by the patient or is not available. However a large study is needed to evaluate the long term outcome of this reconstruction modality.

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CLINICAL TRIAL WITH "ZEETUSS" - A HERBAL COUGH SYRUP IN VARIETIES OF COUGH

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Abstract *Cough originating as a symptom of many diseases can be distressing in its own right. Symptomatic relief from cough is much sought after as seen by availability of plethora of anti-cough medications. Many cough syrups have shown various side effects and thus need to be used with caution in extremes of age, pregancy and lactation etc. The search for a safe and effective remedy prompted the trial of ZeeTuss syrup, a polyherbal formulation in varieties of cough in patients of either sex ranging from 4 to 73 years of age. The duration of treatment was 4-7 days. Routine urine examination and liver and renal function tests were conducted at days 1,3 and 7. Remarkable relief from cough was seen in tracheo bronchitis, asthma in adults and recurrent coughs and cough variant asthma in children. Good results were also seen in chronic bronchitis. It appears that ZeeTuss either suppresses the cough originating from activation of RARs or ZeeTuss effects the central processing of vagal afferents. It is inferred that ZeeTuss Syrup is an effective herbal formulation for symptomatic relief from coughs of varied etiology and free from any side effects or toxicity.*

Key words: *Herbal Medication, Zeetuss; Cough Syrup.*

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Introduction

Many preparations meant to treat cough have their own drawbacks. The most effective antitussive agents, for example, are the narcotic drugs such as morphine, diamorphine, codeine and their semi-synthetic derivaties. Unfortunately at their effective doses, they also cause physical dependance, respiratory depression and gastrointestinal complications. Morphine and diamorphine are very addictive. Non-narcotic antitussive agents have also been developed, but their effectiveness is not fully established. Furthermore, they also have troublesome side effects. The most important non-narcotic antitussive, dextromethorphan, for example, with little higher dose causes dizziness, nausea, vomiting and headache. It has to be used with caution in patients with hepatic insufficiency and those on monoamine-oxidase inhibitors as many cases of central nervous depression and death have occured. Other non-narcotic agents like noscapine, levopropoxyphene, benzonatate, caraniphen and carbertapentane have doubtful value as antitussive agents. Antihistamines are included in several cough mixtures but are of doubtful value.

In this report, the findings of administering ZeeTuss in patients with cough are provided. Table-I describes the wide range of disease processes which may present with cough.

Out of these six groups, the last one i.e. VI, was excluded from the present study and clinical trials with ZeeTuss were conducted on the patients of other five groups, with cough as one of the main symptoms.

Table-I:

Group I	Acute Infections	Chronic Infections
	Tracheo-bronchitis, Broncho-pneumonia, Viral pneumonia, Acute or Chronic bronchitis.	Broncheactasis, Tuberculosis, Cystic fibrosis
Group-II	Airway Diseases	PARENCHYMAL DISEASES
	Asthma, Chronic bronchitis, Chronic post-nasal drip	Interstitial fibrosis, Emphysema
Group-III	Cough Variant Asthma	
Group-IV	Reflux oesophagitis, Recurrent aspiration	
Group-V	Drugs like - Angiotensin-Converting Enzyme inhibitors (ACE inhibitors) induced cough	
Group-VI	Cough accompanying other disease like Foreign body, Tumors (e.g. bronchogenic carcinoma etc), Cardiovascular e.g. LVH, Aortic aneurysm etc.	

Methods

55 patients were divided in 5 groups. The number of patients (n) in each group has been shown in Table-2. The age of the patients varied between 4 to 73 years. ZeeTuss, a herbal preparation in syrup form, was administered to patients according to body weight and age (5 ml to 15 ml), 2 to 4 times, according to severity of the problem.

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TABLE - 2: ANTI-TUSSIVE EFFECT OF ZEETUSS IN DIFFERENT DISEASE CONDITIONS

0 = No effect
Degree of Antitussive effect denoted as +, ++, +++, ++++

Group	Disease	Nature of Cough	Days						
			1	2	3	4	5	6	7
I.	Trancheobronchitis n = 7	FSC+ExC+SpC	0	++	++	++++	++++	++++	++++
	Bronchopneumonia n = 4	FSC	0	0	+	+	+	+	+
	Tuberculosis n = 5	FSC	0	+	+	+	++	+	+
II.	Bronchial Asthma n = 5	ExC+SpC	+	+++	+++	+++	++++	++++	++++
	Chronic Bronchitis n = 5	FSC+ExC	0	0	++	++	++	++	+++
	Interstitial Fibrosis n = 6	FBS	0	0	+	+	+	+	+
	Emphysema	FSC	0	0	0	+	+	+	+
III.	Cough variant asthma n = 7	FSC+ExC	+	++	+++	++++	++++	++++	++++
IV.	Reflux oesophagitis n = 4	FSC	0	0	+	+	+	+	+
	Recurrent aspiration n = 3	FSC+SpC	0	0	+	+	+	+	+
V	Cough induced by ACE Inhibitors n = 4	FSC	0	0	++	++	++	++	++

n = *Number of pts.*
FSC = *Frequent Single Coughs*
ExC = *Explosive Cough*
SpC = *Spasmodic Cough*

After the nature of cough was determined, the number of coughs from day 1 to 7 were counted by independent observers who had no idea of the diagnosis or the treatment. The reports on the number of coughs were only opened when the trial was over.

The patients received antibiotics, ATT or other medications accordinng to disease but no other antitussive preparation (or any bronchodilator in airway diseases) was given. The total duration of treatment ranged between 4 to 7 days in each patient. Routine blood, urine and liver and renal function tests were conducted at days 1, 3 and 7.

Results and Discussion

ZeeTuss was well tolerated by all the 55 patients. No side-effect was found either clinically or in the investigations. The efficacy of ZeeTuss was, however, variable in different diseases according to the groups shown in Table-I.

The results on the efficacy of ZeeTuss have been summarized in Table-2. ZeeTuss had remarkable efficacy in providing relief from the cough associated with acute tracheo-bronchitis but not much in bronchopneumonia and tuberculosis with or without bronchactasis. Similarly, it was highly effective in asthma in adults and in cough variant asthma in children.

A number of factors are responsible for triggering cough. It has been proposed that bronchoconstriction is the primary stimulus. Release of humoral autacoids like histamine, 5HT and other bronchoconstrictors may be involved in the mechanism (Salem and Aviado, 1970). An important pharmacologic action of most antitussive agents is their ability to produce bronchodilatation (Booth, 1988).

Effectiveness of ZeeTuss against bronchitic and asthmatic cough is supported by the findings that the individual constituent herbs i.e. Adhatoda vasica, Glycyrrhiza glabra, Solanum xanthocarpum, Ocimum sanctum and Piper longum showed anti-bronchitic, antitussive, antiallergic and bronchodilatory actions (Amarnath et al, 1989; Bector et al, 1971; Khosla, 1995; Dhanukar and Karandikar, 1984; Tripathi, 1979; Amin and Mehta, 1959; Gupta, 1968). It was reported that S. xanthocarpum has proved useful in treating chronic bronchitis with or without emphysema and non-specific unproductive cough (Bector, 1971). It has also been suggested that the therapeutic efficacy of Piper longum in relieving cough could be due to the suppression of cough reflex (Banga, 1964).

ZeeTuss, on the other hand, elicited fairly good response in chronic bronchitis but not much in interstitial fibrosis and emphysema, which are known as parenchymal diseases.

Mathur (1977) reported that ZeeTuss was uniformly effective in both productive and non-productive cough in patients of pulmonary tuberculosis. He also observed excellent symptomatic relief in coughs of diverse origin and assoociated with bronchitis, bronchietasis etc. These findings throw light on the possible basis of antitussive mechanism of ZeeTuss. It appears that ZeeTuss is more effective in suppressing the cough originating from airway inflamation which mostly occurs due to activation of RARs (Widdicombe, 1998). However, the low efficacy of ZeeTuss in parenchymal diseases may be due to its insignificant effect on type 'J' lung receptors. The role of J receptors is elicited by Singh (1998). Alternatively, ZeeTuss might have been effecting the central processing of these vagal afferents. This possibility must also be considered in future investigations as its effect, how-so-ever small, was also observed on cough induced by ACE inhibitors. The latter are known to influence the pulmonary receptors (Widdicombe, 1998). Depressive action of Adhatoda vasica on vagal terminals on the bronchi was reported (Suresh Kumar, 1981).

The efficacy of ZeeTuss in "Cough Variant Asthma" in children is remarkable and is undoubtedly a new strategy for treating this distressing condition. In children, recurrent cough is a common presenting symptom that may represent asthma. It has been known that children with recurrent cough have increased cough receptor sensitivity or airway hyperresponsiveness (Chang, 1977) only during the coughing phase. The proponents of the entity of cough variant asthma suggest a therapeutic trial with asthma-type medications, including oral corticosteroids for such children (Doan, 1992 and Parks, 1989). Others have proposed the use of bronchoprovocation challenges (Galvez, 1987 and Poe, 1989). Currently, many children with such cough are diagnosed as having asthma and are treated inappropriately (Mckenzie, 1995).

It was suprising that these children had very little response from theophylline and salbutamol corticosteroids. ZeeTuss was found very effective in such cases. Effectiveness of ZeeTuss against cough variant asthma could be due to the synergistic effect oof antiallergic and bronchodilator plant principles. The only preparation that enhanced the efficacy of ZeeTuss was antihistamines viz. cetrizine (Alerid) syrup. The exact mechanism, however, remains so far unknown. It was reported that a specific glucoalkaloid from S. xanthocarpum provided significant protection against antigenic challenge with a concomitant decline in lung tissue histamine and 5 HT content (Gupta, 1967). Combination of leukotriene antagonists and antihistamines have been found to be highly effective in asthma (Roguet, 1997). It appears therefore important to see whether ZeeTuss acts through the 'leukotriene pathway'.

All pharmacological agents that increase intracellular levels of cyclic AMP have been shown to inhibit the release of autacoids from lung tissues, basophils and mast cells (Orange, 1971; Loeffller, 1971; Tayloor, 1974; Kaliner and Austen, 1974). Glycyrrhiza glabra has been shown to inhibit cAMP phophodiesterase activity and thereby increase intracellular cAMP levels (Thein, 1995). Moreover, the alkaloids obtained from Adhatoda vasica were observed to have powerful antagonising effect against histamine induced bronchospasm (Cambridge, 1962). These may have contributed to the combined effect of ZeeTuss and antihistaminic cetrizine.

Conclusion

ZeeTuss is an effective antitussive agent in airways diseases, free from any side-effect or toxicity. The efficacyof ZeeTuss is remarkable in children with "Cough Variant Asthma". ZeeTuss can be successfully used for "Recurrent Cough" in children which continues to remain a diagnostic and management problem. However, the antitussive effect of ZeeTuss is comparatively low in parenchymal diseases or chronic infections. Though some insight is now available but mechanism of action for antitussive effect of ZeeTuss remains to be elucidated.

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GUIDELINES FOR THERAPEUTIC MONITORING ON ANTI EPILEPTIC DRUGS

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International League Against Epilepsy and Commission on Antiepileptic Drugs has laid various guidelines on Antiepileptic therapeutic drug monitoring (TDM)(1). In this article the author has attempted to summarize these recommendations in optimising antiepileptic drug (AED) therapy by measuring drug concentrations in body fluids as an aid to the management of epileptic patients receiving drug therapy for the cure, alleviation, prevention of disease and for individualisation of drug therapy.

Rationale for Therapeutic AED Monitoring

The dose of some drugs is fully satisfactory in some persons, causes toxicity in others and has little effect in some. Therapeutic Drug Monitoring (TDM) has developed over the past 20 years and its main aim is to maximize the benefit of a prescribed drug and at the sametime minimize toxicity. Prior to TDM, the drug dosing was based on dose response relationship. Clinicians individualized the therapy for the patients by increasing the dosage based on interpretation of clinical response. Though this trial and error method was tolerated for a number of drugs, it was found that therapy with certain drugs could be improved e.g. patients on phenythoin therapy (8-20%) showed signs of toxicity. Mortality among toxic patients ranged from 7-50%. Although TDM for AEDs has been routinely practised in clinical laboratories since the mid-1970's, the scientific foundations of the subject can be traced to the 1960's, when Buchthal and Svensmark(2) showed that there was a relation between plasma concentrations of phenytoin in patients being treated for epilepsy and the degree of seizure control attained. This was later extended by other investigators to other AEDS and these observations permitted the assumption that a direct relation exists between the efficacy of a given AED and its concentration at its site of action. Some of the most important observations are as follows:-

1. Most patients are improved when the blood level of the AED is in a certain range, a range which differs for each AED and which is usually called the therapeutic or the optimum range. Blood levels higher than the therapeutic range are usually associated with signs and symptoms of toxicity i.e. the toxic range. A good correlation between blood and brain level of several AEDs has been documented.
2. Analysis of blood level data from large group of patients has shown that most patients attain levels in an expected range depending on the given dosage of the AED; but wide variations in blood levels are observed at a given AED dosage between individual patients. The correlation between level/efficacy or level/toxicity, therefore, is much better than the correlation between dosage/efficacy or dosage/toxicity so the dose response approach was replaced with serum drug concentration response.
3. There are many factors (mentioned below) which influence the blood levels of AEDs, and for all these reasons, blood monitoring of AEDs is important.
    a) ***Intake of AED:*** The first potential problem affecting the relationship between the prescribed dose of AED and clinical effect is the question whether the patient actually takes the drug as prescribed. If an adequate dosage is prescribed by the physician, the most frequent cause of low blood levels (and occassionally toxic levels) is failure of patients to ingest medication as prescribed. Such poor compliance is frequently denied by the patient, and can be easily detected by measurement of drug concentrations in body fluids.
    b) ***Absorption:-*** Rate and extent of absorption is affected by the biopharmaceutical formulation and differences between non-generic and generic preparations. Once a drug has been taken, the next potential source of variation is in the amount of the dose which reaches the systemic circulation. This varies not only between drugs but between individuals and between different dosage forms of the same drug. AEDs are marketed in solutions, syrup, standard tablets enteric coated tablets, slow

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release tablets and suppositories. A classical examples of where an apparently small change in the formulation of the drug led to large changes in bioavailability and consequently major changes in plasma concentration and clinical effect was seen with phenytoin in Australia in 1968. The cause was traced to a change in the excipient used in a particular brand of phenytoin, leading to marked increase in plasma concentration of phenytoin. Other important factors in absorption include gastric content, gastrointestinal disorders and co-administered drugs.

c) ***Binding to plasma proteins:*** Protein binding differs for each drug but normally is quite constant for one AED in the same patient. A reduction in binding can have clinical consequences with highly protein bound AEDs such as PHT or valproic acid (VPA). The free fraction of the AED can be increased if hypo-albuminemia occurs or if co-administered drugs displace the AED.

d) ***Metabolism:*** AEDs are metabolized by microsomal hepatic enzymes. Most discrepancies between dosage and blood levels arise at this site. Metabolism is saturable or nonstaturable. For many AEDs, elimination is proportional to dosage, but for others such as PHT, it depends on enzyme saturation. Above a certain threshold, zero-order kinetics may appear leading to an overproportional increase in plasma concentrations. The capacity of hepatic enzyme is genetically determined. Some patients have very low oxidative metabolism, in others it is rapid. The capacity of hepatic enzymes also depends on age. It is very slow in newborns, faster in children than in adults and again slower in elderly patients. The activity of the hepatic microsomes can be modified by numerous drugs either enzyme inducers or enzyme inhibitors. These variations may be important particularly for AEDs with significant first pass metabolism.

e) ***Excretion:*** AEDs modifying urinary PH or renal insufficiency can impair renal excretion.

f) ***Elimination half life*** (t½) and timing of daily dosage. Wide variations in blood levels occur with administration of AEDs with short t½ or administration in one or two daily doses if controlled release preparations are not used.

g) ***Patient's body weight.*** Errors in measurement or sudden change in patient's body weight can lead to miscalculation of daily dosage.

h) ***Volume of distribution:*** The volume of distribution is modified by age, weight changes, and pregnancy.

When should blood levels of AEDs be measured?

Indiscriminate use of blood level determination is not recommended. Logic and Clinical judgement must be used in deciding when measurements are to be made and how to use the information obtained. Use of blood levels to adjust dosage so that numbers fall within the "therapeutic range" is a waste of time and money and may even be dangerous if effective and well tolerated therapy is changed simply because levels are not in the published ranges. It is better to develop a target range for each patient based on severity of epilepsy and tolerance of side-effects.

1. Routine determination in all patients receiving AEDs has been suggested on theoretical grounds.
   - i) After initiation of AED therapy, usually some weeks later, to confirm the first value.
   - ii) Once or twice yearly to verify compliance.
   - iii) After each change in AED regimen (change to dosage, or change of AED or other medication.
2. TDM in special situations with special purposes.
   - i) When a patient complains of toxic sign possibly dosage related.
   - ii) To differentiate between non compliance and true drug resistance, when seizures are not controlled despite an adequate prescription.
   - iii) When a patient receiving an AED exhibiting zero order kinetics where a small increase in dose will produce a disproportionate increase in plasma concentration e.g. phenytoin under special physiological and pathological conditions is likely to alter drug pharmacokinetics e.g. pregnancy, anemia, hepatic and renal insufficiency.
   - iv) Possible drug interaction - Patients receiving antiepileptics with antitubercular drug.

3) ***NEVER***

When and where blood level determinations of AEDs are impossible or unreliable, unrealistic or empirical dosage adjustment is a satisfactory alternative. In pharmacoresistant patients, AEDs must be prescribed to the maximally tolerated dose without importance to the upper limit of therapeutic ranges.

Practical guidelines for effective TDM

1. Sample collection:

This requires that the sample be collected after steady state levels have been reached because prior sampling will cause the prescriber to dangerously increase the dose. The only time samples need not wait for a steady state is when drug toxicity is suspected. The time taken to reach steady state is determined by the elimination half life of the drug and steady state is reached, after approximately five half lives. For drugs with a narrow therapeutic window, the sample may be collected after two half lives.

2. Timing of sampling:

Generally samples are collected well after the last dose (pre-dose, just before the next planned dose) in trough levels. For drugs having long half lives (e.g. phenytoin) the timing of sampling is not very critical. For drugs having short half lives and diurnal kinetic variations (Carbamazepine in children) samples should be collected at a fixed time. Trough levels are best indicators of drug efficacy whereas peak levels are more relevant in the diagnostic of toxicity. Peak level samples for I.V. bolus injection should be collected from the opposite arm 20 to 30 minutes after I.V. injection and 30 to 60 minutes after I.M. injection.

3. Drug estimation procedures:

In order to improve the situation, an attempt was made in 1960's to integrate clinical pharmacokinetics and laboratory technology with clinical medicine. So accurate reproducible methods for determining serum drug concentrations of AEDs were evolved on spectrophotometry gas liquid chromatography (GLC), high pressure liquid chromatography (HPLC) or radioimmunoasay. HPLC is a procedure which requires considerable technical experience, but for which recurring cost is the least. Radioimmunoassay does not require too much technical expertise and several samples can be processed at a given time. The recurring cost of RIA is however high. In 1970 EMIT and fluorescence immunoassays were developed and found to be accurate and reproducible as well as rapid and simple to perform.

4. Interpretation of plasma concentration data:

Therapeutic concentrations are average values and individual patients will show satisfactory drug response at levels above and below the therapeutic range. Plasma concentration data must act as adjuncts to therapy and concentration data must always be considered in light of the patients clinical response.

5. Dosage adjustment after TDM:

For drug with linear kinetics, increasing the dose leads to a proportionate increase in plasma concentration and can be safely carried out (phenobarbitone, carbamazepine). For drugs with non-linear kinetics, relatively small increase in dose can result in disproportionally large increase in plasma concentration (e.g. phenytoin). For such drugs it is desirable to use nomograms to guide dosage adjustments.

Recommended procedures for TDM

1. Check any prior relevant drug therapy that the patient has received.
2. Compare this with serum drug concentration levels obtained and any manifestation of drug efficacy or toxicity.
3. Establish reason for present monitoring.
4. Document relevant patient factors.
5. Review relevant pharmacokinetics of drug being monitored.
6. Determine the amount and route of dose given.
7. Determine the time of dose given.
8. Document sampling time.
9. Interpret serum drug concentration as sub-therapeutic, therapeutic or toxic by considering the pharmacokinetics and clinical effects of the drug.
10. Design proper dosing regimen in consultation with physician.
11. Outline a follow up as to when future serum drug concentrations are required.

Therapeutic drug monitoring and Pharmacoeconomics:

The ever increasing rate of inflation and the reality that resources for medical care are limited, has led to economic evaluations of several health care services including therapeutic drug monitoring. TDM for anticonvulsant drugs was introduced for the first time 25 years ago and at that time, had a major impact on improving the effectiveness and safety of anticonvalsant therapy. Since then a few cost benefit and cost effectiveness evaluations of TDM in epilepsy have been carried out and one study has shown better rates of seizure control in patients monitored regularly in the first 6 months of their epileptic character, but not if the monitoring began later than 6 months. Our own study(4) of the cost benefit of this service showed that of 70% of patients achieved either partial or full seizure control after regular anti-convulsant drug level monitoring. There was wide individual variation in plasma concentration of phenobarbitone and phenytoin at steady-state.

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NEWER TRENDS IN PEDIATRIC NUCLEAR MEDICINE

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Pediatric diseases often differ significantly from those of adults. While diseases such as infections and cancer do occur in children, there are also unique diseases in the pediatric age group. Nuclear medicine techniques are applicable in the diagnosis of a wide variety of pediatric diseases. In this brief review, I would like to highlight some of the more important applications of nuclear medicine techniques to children. There are those who might believe that the use of radioactive materials during childhood would be dangerous. Actually, the use of certain nuclear medicine techniques results in a lower radiation exposure to the child than conventional radiological techniques. The principle of risk/benefit ratio always applies in the use of radiation. In evaluating childhood diseases this is particularly the case. Whenever nuclear medicine techniques are employed, the benefit to the child in question must be judged to be greater than the small potential risks.

Newborn children may have abnormalities (malformations) of their kidneys. These problems may result from faulty development during pregnancy. Some of these malformations do not cause serious complications. However, others may result in one or both kidneys having abnormal function or urine flow. When a structural abnormality is discovered in a baby's kidney or laboratory tests suggest that the kidneys are not operating correctly, a nuclear medicine study is commonly performed.

One of the more common developmental abnormalities in children is partial or complete blockage to the flow or urine from the kidneys. This results in enlargement of the affected kidney and may cause the child pain or be found by the doctor during a routine examination. Standard x-ray studies may demonstrate enlargement of the kidney. However, there are other problems that may simulate blockage of urine flow. When blockage of urine flow is suspected, the child may be evaluated by nuclear medicine diuretic renography.

Renography utilizes a radiopharmaceutical that follows a portion of the normal pathway in urine production (MAG3). The kidney usually excretes this radiopharmaceutical quickly. When there is a blockage to urine flow this material accumulates in the affected kidney. If a patient has suffered kidney infections previously, the kidney may be enlarged and urine flow may be slow. This may appear to be an obstruction, when in reality none is present. By combining a diuretic (a drug that increases urine flow) with the renogram, urine flow is increased during the test. If the MAG3 is cleared from the kidneys after administration of the diuretic, surgery may not be necessary. However, if the test shows a failure to clear the material from the kidneys after diuretic administration, surgical correction of the obstruction may be required.

In children with impaired kidney function the actual contribution of each kidney to total urine production can be measured. If it is necessary to remove one kidney,the physician can predict in advance whether the remaining kidney has sufficient function to sustain the child. Children with impaired renal function may be monitored over time by nuclear medicine procedures. This monitoring may indicate whether the disease is improving or deteriorating.

It is important that the child have adequate fluid intake prior to the test. If the child fasts, then he or she may become dehydrated after the administration of the diuretic. Not only does this mean discomfort for the patient, it alters the reliability of the examination.

Children tend to suffer urinary tract infections more commonly than adults. In some of these patients the infections become frequent. One of the predisposing factors to such infections is reverse urine flow (reflux) from the bladder to the kidneys. This condition is referred to as vesicoureteral reflux. Many children will grow out of the condition without any surgical therapy. However, others will have repeated infections that lead to discomfort and potential kidney damage. If the child fails to grow out of the condition, or the infections become too frequent, surgery may be required to reimplant the ureter.

In order to monitor the progress of the patient, and to confirm the diagnosis of reflux, an objective examination is required. The nuclear cystogram has been developed particularly for use in monitoring both the presence of reflux and the effectiveness of the therapy in children. The test may be performed in the outpatient setting. There is some mild discomfort associated with this examination since a small tube (catheter) must be threaded into the

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urinary bladder.

Once the tube is in place a salt-water solution and radiopharmaceutical mixture is administered via the tube into the bladder. If reflux is present, the monitoring device, a gamma camera, can detect it. Computers make it possible to determine the degree of reflux as well. While similar tests are available in diagnostic radiology, the amount of radiation administered to the patient may be 100 times that administered during a nuclear medicine examination. Because of the low radiation dose children can be monitored periodically to see whether the reflux is resolving spontaneously.

No specific patient preparation is required. The patient is not required to perform any particular maneuvers during the examination. It is often beneficial for the patient and parent to remain together during the study. If the parent can exert a calming influence on the child then the examination will go quickly with little discomfort.

One of the diseases that may be seen in the pediatric age group is neuroblastoma. This tumor usually arises from the region of the adrenal gland. However, it may arise elsewhere in the body as well. It is important to know the location of all sites of disease. Conventional imaging methods such as computed tomography (CT) may identify the primary tumor. However, small tumor deposits elsewhere may not be seen. In order to determine the appropriate therapy for a neuroblastoma patient, as many sites of disease as possible should be identified.

In order to identify these sites, a radioactive compound, MIBG, is used. Normally a portion of the adrenal gland concentrates MIBG, but it is also concentrated by neuroblastoma. The location of the neuroblastoma does not affect MIBG uptake. Therefore, disease sites other than the origin of the tumor can be identified. The use of radioiodine-labeled MIBG has proven to be of significant benefit in determining whether neuroblastomas spread. In addition, by locating as may sites as possible at the time of diagnosis, this examination can be used to evaluate how effective therapy is. The disappearance of previous sites of disease and the lack of appearance of new sites, suggests that therapy is effective. However, when disease persists and is identified on the scan the outlook for the patient is diminished.

Little patient preparation is required for MIBG studies. This material is usually administered by intravenous injection. There are very few substances that interfere with MIBG. However, because MIBG can accumulate in bowel at times, laxatives may be required for delayed imaging. Normally, MIBG is imaged between 24 and 48 hours after injection. Imaging sessions may take as long as an hour or more. Young children may have to be sedated so that they do not move during the imaging.

Three phase bone scan has already established its role in prompt diagnosis of osteomyelitis. While this application exists in children, there are a number of benign orthopedic conditions, in which bone scanning may be useful. Children who are experiencing pain that appears to be bony in origin may have infections, trauma, or other orthopedic diseases.

Spondylitis is an inflammation of a vertebral body in the spine. Spondylolysis represents the separation of a portion of a vertebra. Both of these conditions are commonly seen in children, particularly those who are athletic. When children suffer from back pain and standard x-rays are normal, then bone scanning is usually indicated. The same may be said of children who suffer from pain in their legs. Stress fractures represent incomplete breaks in the bone. They are often painful and are commonly seen in those who run as part of an athletic event. The bone scan identifies the majority of stress fractures, even those not identified on plain x-rays.

Unfortunately, in today's society child abuse is a reality. The documentation of the abused child is often difficult. When multiple healing fractures are identified on x-ray, child abuse is suspected. However, it takes a period of time for these fractures to appear. The bone scan can rapidly identify the same or even more sites before there are many x-ray changes. Abused children can therefore be diagnosed soon after the incident. When the bone scan demonstrates many rib adnormalities or areas of increased concentration in the long bones, child abuse may be suspected.

Infections of the bone in children are not uncommon. The bone scan, performed with some special additional views, can make the diagnosis within twenty-four hours of the onset of the disease. This allows rapid treatment with antibiotics. Today, patients who have been scanned for the diagnosis of bone infections may be treated so effectively that their x-rays never show any change.

Pain in the hip may represent a specific disease of childhood known as Legg-Perthe's disease. In this disease the upper portion of the hip starts to degenerate. This may lead to collapse of the entire hip. The early changes of this disease can be seen on the bone scan and the progress of both the disease and healing may be monitored. No specific preparation is required for bone scanning.

During the preteen and early teen years the testicle may twist on the blood vessels feeding it. This is known as testicular torsion. Generally, the boy complains of significant pain in the groin or testicular region. There may or may not be swelling present. The usual treatment for torsion is surgery. However, there is another disease that may mimic torsion. This disease, epididymitis, is a inflammatory disease of a structure near the testicle. It is generally self-limited or may respond to antibiotics. However, surgery is not usually employed in this condition.

Using nuclear flow studies testicular torsion can be separated from epididymitis. In testicular torsion the flow study shows decreased flow (a negative defect) over the testcile. However, in epididymitis there is increased flow early after the onset of pain. It is important that children complaining of pain in the testicle be seen by a physician quickly to determine whether or not further diagnostic studies or therapeutic interventions may be required.

Summary

I have reviewed above only a few of the pediatric nuclear medicine studies. Pediatric nuclear medicine offers many diagnostic opportunities to solve clinical problems in children. In order to properly perform examinations individuals trained in this subspeciality area should be available. When a physician recommends a pediatric nuclear medicine examination, there should be little hesitation in studying the child. There is an excellent safety record with regard to long-term outcome in children. Radiation doses are low and present little risk to the child. The risks of not studying a child by nuclear medicine examination are much greater than any radiation risk.

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BILATERAL PALATAL CANINE IMPACTION:

An impacted tooth is one that has been prevented from eruption and thus does not come in proper occlusion, by some physical barrier in the path of eruption[1,2] Viz. adjacent teeth, overlying bone or fibrous tissue. Maxillary Canines are the most frequently impacted teeth after the third molars. Palatal impaction of Canine is 3 times more common than buccal and unilateral is more frequent than bilateral impaction. The reason for their high incidence of impaction is that they start their development at a higher level and erupt after the adjacent teeth[3].

Careful Radiographic Examination of an un-erupted Canine is essential before deciding upon treatment because unlike a wisdom tooth it may be possible to uncover the tooth to permit its eruption into the arch and thus achieve normal occlusion and aesthetics. The radiographs required include:-

Periapical: It shows degree of root formation of Canine, apical curvature, any root resorption affecting adjacent teeth and presence of an associated cyst.

Occlusal Projection: Provides buccopalatal localization of the Canine and determine its relationship to the standing teeth.

Parallax Method (Buccal Object Rule): For determining whether the tooth is located palataly or labially.

OPG: For demonstrating the vertical angulation of the tooth and its height above the alveolar margin.

Lateral sinus view: For three dimensional localization.

P.A. projection (water's): to rule out sinus involvement.

As the maxillary cuspids have the longest period of development and the most torturous route to come into full occlusion, they are the next most frequent impacted teeth after the third molars. These impactions occur more frequently in females than males. During the formation of its crown, the cuspid remains posterior to the anticipated eruption path and it gradually assumes a more vertical alignment before eruption at about 11 to 12 years of age. Deviation from the the normal eruptive position usually results in palatal inclination thus terminating in an impacted state. The maxillary cuspids must both erupt between teeth already in place and compete with the second molars for dental arch space[4,5].

The causes for Canine impaction include:

1. Although most Canine impactions occur in dentitions without crowding, however svere space loss or crowding can be causative factor.
2. Ectopic position of the tooth germ.
3. Delayed resorption of primary Canine.
4. Lack of guidance from the gubernacular canal.
5. Root tip deflection.
6. Hereditary.
7. Congenitally missing lateral incisor.
8. Obstructed eruption path e.g. by supernumerary tooth or odontomas.
9. Trauma.
10. Cleft lip and palate deformity.

Due to the severity of problems related to canine impaction careful supervision and early diagnosis of eruption disturbances are important.

Clinical inspection and palpation of the alveolar process in the canine region is recommended annually from the age of 8 years.

The indication for radiographic diagnosis before 11 years of age (10-11 years of age is critical period in the maxillary canine eruption) are:-

1. Difference in eruption of the maxillary canine between the right and left sides.
2. The canine cannot be palpated by the age of 8-10 years.
3. The Central incisor is late in eruption.

4. The lateral incisor shows a pronounced displacement or labial tipping.

Indications after 11 years of age are:-

1. All individuals with un-erupted and non palpable canine with otherwise normal dental maturity.

Treatment:-

Surgical removal is the usual option for managing impacted canines[6,7]. The other modalities of treatment which some times suffic include:-

1. Surgical exposure in preparation for orthodontics.
   - Provided the patient is of young age.
   - Position of root apex is favourable.
   - There is enough space at the proper place in the arch
2. Surgical repositioning.
   - Same above 3 provisions.
3. Transplantation.
4. Leaving in situ:- provided the patient is asymptomatic, radiographicallly there is not any bony pathology or when patient is a surgical risk.

The Radiographs presented in this letter belong to a 16 years girl who reported to the department of Oral and Maxillo - Facial Surgery. Govt. Dental College Srinagar with complants of.

1. Abuse of 3/3 from the arch and
2. Retention of C/C.

Clinical examination of the Palate of the patient revealed 2 small bulges just posterior and lateral to the incisive papilla. This particular case was treated by surgical remonal of both the canines by palatal approach.

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A STUDY OF WAITING TIME ON THE OUTPATIENT DEPARTMENT OF TEACHING HOSPITAL

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Introduction:-

Queuing or waiting line problems are concerned with the design and planning of facilities to meet a randomly fluctuating demand for service. If service facilities are not adequate to meet demand this leads to congestion at the service facilities and incurs certain associated costs. However increased service capacity to reduce congestion usually causes increased idleness in the service system. This includes a cost of idle service facilities. Waiting line problems usually strive to design systems that balance the aggregate costs of idleness and congestion and minimized the total cost of services system. Analysis in this problem area of health research has been more extensive and probably more sophisticated than any other. Hospital system can be viewed as large and complex service facility outpatient department as service facilities has been analyzed. Congestion occurs in the form of waiting lines of patients. Increasing the capacity of hospital may cause increase in the idle service facilities in the form of idle beds, excess staff and other services.

Health administrators are continuously faced with questions concerning the number of servers to be employed on full time basis and a variable work load having to assess, the impact of heavy service load and variable arrival rate on hospital facilities in order to justify any additions. They have also to see the extent upto which service rate can be improved, so as to provide equal satisfaction to the patients even in case of increased arrival rate. The scope of queuing theory seems to be wide and several models can be applied in OPDs, depending upon arrival and service patterns. Whenever there is a flow of patients requiring service, a queue may have to be formed and patients have to wall of their service as every one can not be served simultaneously, so it can cause congestion and waiting lines have to be formed to maintain proper discipline i.e., FCFS (first come, first serve).

Efforts have been made in this paper to introduce queuing theory to provide answers to the above questions in hospital management and such a study can help in the operations research with its wide scope and several models can be applied in OPDs depending upon arrival or service patterns.

Objectives

To find out the average waiting time of outpatients at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar.

To find out expected waiting time and suggest remedial measures for optimization of the system keeping in view effectiveness/efficiency by utilizing the simple queue discipline FCFS (first come, first serve) excluding priorities.

Methodology

The study was undertaken in the outpatient department of the Sher-i-Kashmir Institute in the Polyclinic area. An observation study conducted on 100 outpatients which were randomly selected for such a study on all working days between 10 a.m. to 1 p.m. The patients selected were followed right from the time to entry upto the registration, was observed till he went into the consultation chamber irrespective of the speciality, till he left the area after getting investigations done if required and final timing noted at the exit point. The queue serials with actual waiting number of the patients were routine and not by appointment as in referral clinics which have been excluded in the study. About 100 patients in total were observed: 60 in surgical speciality and 40 in medicine speciality. Various timings were calculated and average waiting time worked out by the formula.

$$\frac{\text{Total Waiting Time in Minutes}}{\text{Total Number of Patients}}$$

For record purpose, timings were noted right from entry upto obtaining outpatient card and queue timings noted at consultation, investigation and exit point. For that purpose various proforma were developed, pretested and standardized their acutal application.

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TABLE-1:

	Speciality	Total patients under study	Total time calculated	Average waiting time
From entry point to reach consultation chamber	Medicine	40	1282 min.	32.05 min.
Consultation time (from entering the cubicle to leaving the chamber)	Medicine	40	1782 min.	44.55 min.
From consultation cubicle upto Lab+ Exit Q3	Medicine	40	785 min.	19.62 min.
Total		40	3949 min.	96.22 min.

Waiting time calculated:
Minimum = 37 minutes
Maximum = 156 minutes

TABLE-II:

	Speciality	Total patients under study	Total time calculated	Average waiting time
Q1 From entry to consultation chamber (cubicle)	Gen. Surgery	60	2356 min.	39.2 min.
Q2 From entering consultation cubicle upto leaving consultation chamber	Gen. Surgery	60	2207 min.	36 8 min.
Q3 After concultation to Lab. or Exit	Gen. Surgery	60	1177 min.	19 6 min.
Total		60	5740 min.	95.66 min.

Waiting time calculated:
Minimum = 43 minutes
Maximum = 158 minutes

Observation and Discussion

The study undertaken in the outpatient department of SKIMS on randomy selected 100 patients (40 from General Medicine and 60 from General Surgery) were routine and non-appointment patients and results are depicted for Medicine and Surgery patients in Table I and II Pie- Chart (Fig I & II).

Out of 40 patients in Medicine the total waiting time of patients right from entry point upto the exit point was calculated as 3849 minutes and average waiting time calculated by the formula:

$$\frac{\text{Total waiting time in minutes}}{\text{Total number of patients}}$$

which was worked as 96.22 minutes (1 hour 36 minutes ± 22 seconds) with a minimum waiting time 37 minutes and maximum waiting time156 minutes. Out of 60 patients from General Surgery total waiting timing calculated was 5740 minutes and average waiting time calculated was found as 95.66 minutes (1 hour 35 minutes ± 6 seconds) with minimum waiting time 43 minutes and maximum waiting time 158 minutes and the same formula was used as above.

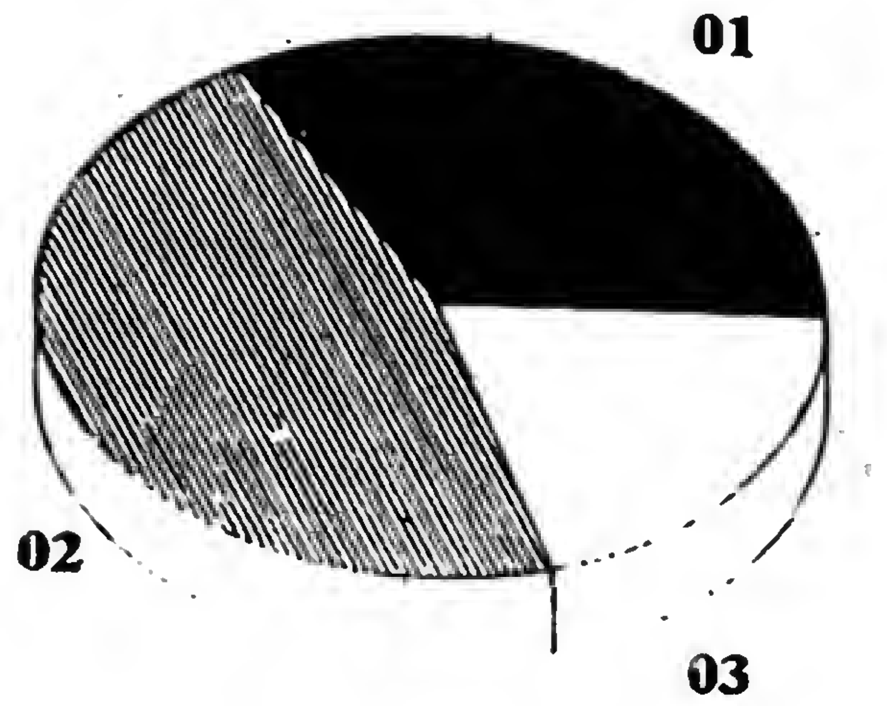

Fig. I:

While comparing the results with that of SN Children Hospital Allahabad conducted in June 1988 on paediatric patients totalling 1764, with clinic timing 8 a.m. to 2 p.m., the study conducted by Joshi et al showed mean waiting time of these patients as 23.93 minutes the average waiting time of the out patients is definitely more in SKIMS, than that of Children Hospital Allahabad.

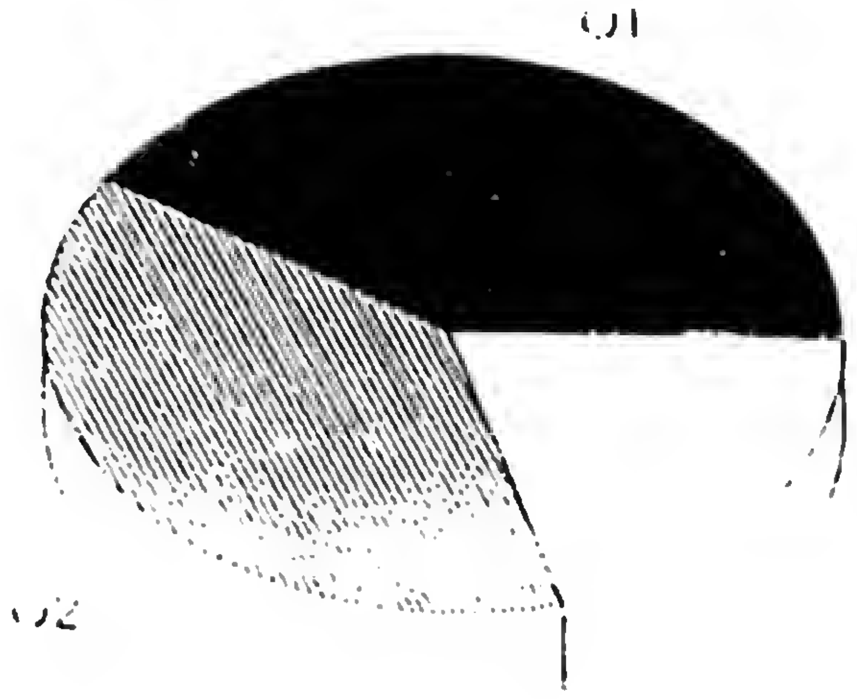

Fig. II:

The Factors Influencing Waiting Line

1. As compared to non-appointment clinic registration counter White OPD cards (Poly clinic) are distributed from one counter and appointment clinic green cards (Referral clinic) are from two counters and shows that medical record technicians are less as compared to

huge rush of patients.

2. Out side the consultation chambers, again the congestion increased and number of attending doctors is just 1-3 Junior Residents/PGs/Senior Residents.
3. Outside laboratories or X-ray, ECG Labs, again congestion causes delay in the disposal of patients.
4. Clinic time in Allahabad Hospital started at 8 a.m. to 2 p.m. unlike that of SKIMS which is 10 a.m. to 1 p.m.

Recommendations

1. In order to maintain proper queue, security personnel should be deployed to maintain peace and discipline i.e., first come first serve (FCFS).
2. Number of medical record technicians should be increased to cater to the huge number of patients.
3. Number of Resident Doctors need to be increased to cater to high rush of patients.
4. All the queues whether for registration centre, consultation chamber or laboratories etc., preference should be given serial-wise excluding priorities.
5. The clinic time should be accordingly increased so that the patients are uniformly attended to and to the patient's satisfaction.
6. If possible afternoon clinics be started so that the patients not attended could be tackled in afternoon clinics probably 2 p.m. to 4 p.m. would be ideal.
7. Social attendants/guides meant for guidance/ information of OPD patients were lacking and should be recruited.

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DECISION MAKING IN MANAGEMENT OF ASYMPTOMATIC CAROTID ARTERY STENOSIS.

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Several clinical trials regarding carotid endarterectomy for asymptomatic carotid artery stenosis have been conducted in the past two decades. These trials have still not resolved the controversy regarding the optimal treatment of such patients. Factors such as the degree of the stenosis, patient comorbid factors and the hospital and surgeon specific peri-operative morbidity and mortality contribute significantly to the success of the surgical procedure. The workup must carefully balance risks associated with carotid endarterectomy against risks of nonsurgical treatment.

CASE PRESENTATION 1:

A 65 year old male comes for a routine physical checkup. During the examination, a bruit was heard over the left common carotid artery. Rest of the physical examination was normal. The duplex doppler ultrasound testing showed 80% narrowing of the left internal carotid artery. The right carotid and vertebral arteries were normal.

From the above presentation it can be concluded that the patient is having carotid atherosclerotic disease. If the patient was symptomatic, the treatment was carotid endarterectomy. Although surgery carries such risks as stroke, myocardial infarction, transient ischemic attack and even death, still the risk of debilitating stroke from symptomatic carotid artery stenosis far outweighs the risks of surgery. However in the above case the patient is asymptomatic and the brain ischemia caused by carotid artery stenosis may have escape medical attention partly because the patient could not attribute the symptoms correctly. Hence the internist should ask specific questions about the ischemic events and repeat them every time the patient comes for follow up visits. The patient should be asked if ever he had greying or fogging of vision or sudden decrease in vision. He should also be asked about any episodes of peripheral numbness, tingling or clumsiness in any of the limb.

Assuming that the patient does not have any comorbid conditions that may increase the surgical morbidity and mortality, the patient is advised for strict risk factor reduction if he has any and to undergo carotid endarterectomy by a surgeon who has extensive experience with carotid surgery and has a very low morbidity record. Further the procedure should be carried out in an medical center which has very low peri-operative morbidity and mortality rate.

CASE PRESENTATION: 2

A 69 year old male who had to undergo angiography for his coronary artery disease was found to have a bruit over the left carotid artery. The patient has a past medical history of coronary heart disease and hypertension. There is no history of diabetes mellitis or hypercholesteremia. The duplex doppler examination showed 70% narrowing of the left internal carotid artery. The right carotid and vertebral arteries were normal.

The treatment of the above asymptomatic patient remains controversial. Although the Asymptomatic Carotid Atherosclerosis Study (ACAS) has recently shown that surgery was more beneficial than medical therapy in men with greater than 60% stenosis, other factors have to be taken into consideration while making decision about surgery. The surgery should be done in such a medical center where the hospital and surgeon specific peri-operative morbidity and mortality is very low (2.3%). The patient has a past medical history of coronary heart disease and hypertension which increase the surgical risk. The patients likely five year survival rate should also be taken into consideration while making decision about surgery. Lastly the decision for or against surgery should be made mutually by the patient and a physician who is experienced in treating cerebrovascular disease. Such conditions as atrial fibrillation, hematological disorders or peptic ulcer disease can affect the decision to use anti-platelet therapy. It is the physician responsibility to share and interpret the evidence with the patient and to offer him all the possible options.

CASE PRESENTATION 3:

A 79 year old female presented to the omini clinic for her routine physical examination and refills for her blood pressure medication. She has no past medical history of

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coronary artery disease, diabetes mellitis or hypercholesteremia except for well controlled hypertension. On examination her internist heard a bruit on her right carotid artery. The duplex doppler ultrasound showed 60% narrowing of the right internal carotid artery. The left carotid and vertebral arteries were normal.

The treatment in the above asymptomatic case should include control of high blood pressure, anti-platelet therapy and monitoring of the carotid arterial lesion with doppler ultrasound for further progression of the lesion. From the results of ACAS in surgical group the five year stroke reduction in women was 17% and in men it was 66%. It was found that women have higher perioperative complication rate. Hence medical therapy is the best treatment for the above case.

DISCUSSION:

Carotid endarterectomy (CEA) was first performed in 1954, and by 1960 it became a popular surgical procedure for the prevention of embolic stroke. It was found that 53% fewer strokes would occur if individuals with 60% or greater stenosis were submitted to CEA[1]. The CEA was initially used as prophylaxis against ischemic stroke in symptomatic patients but with the awareness of carotid bruits along with non-invasive techniques for diagnosing carotid stenosis and reduced peri- operative mortality from both the surgeon and the medical center where it was performed, CEA was been performed for selected asymptomatic patients also.The prevalence of asymptomatic carotid stenosis ranges from 0.5% in people under 60 years of age to 10% in those over 80 years of age[2]. It was found that more strokes present without warning symptoms of transient ischemic attacks (TIA) and the question was which group of asymptomatic patients with carotid stenosis should undergo CEA. This lead to various multi center trials evaluating the efficacy of CEA in asymptomatic patients. The randomization of patients was based on medical management or CEA followed by medical management.

The Asymptomatic Carotid Atherosclerosis Study (ACAS) began in December 1987 and was supported by National Institute of Health (NIH). It was a prospective randomized multi-center trial and the results of this trial were stopped early based on mean follow up of 2.7 years which was statistically extrapolated to a 5 year follow up time[3]. The participating surgeons had to meet stringent criteria demonstrating a perioperative complication rate of less than 3%. The patients with TIA or stroke or with history of endarterectomy were excluded. Overall, the risk reduction was 53% in surgical group. The five year stroke risk reduction in men was 66% and in women it was 17%.

This discrepancy could be related to a chance finding due to small number of women in the trial and also the perioperative complication rate for women was 3.6% which is double than men (1.7%). The 30 day morbidity and mortality rate of ACAS patients was 2.7%. In patients with 60% or more stenosis the medical group showed a stroke rate of approximately 2% per year, which was reduced to approximately 1% per year for the surgical group. The relative risk ratio showed a benefit of over 50%, which is substantial for the surgical treatment. The absolute risk reduction was only 1.5%. The sample size in ACAS was not large enough to address prevention of major or minor stroke[4]. There is no evidence to suggest that CEA has prevented serious or debilitating strokes in asymptomatic carotid artery stenosis patients. Further there is a risk of 0.2% major stroke rate if patients have to undergo angiography.

It was found that six symptomatic patients with severe stenosis need to be subjected to CEA to prevent 1 stroke in a 2 year period but 67 asymptomatic individuals need to undergo CEA to avoid 1 stroke in a 2 year period[1].In ACAS trial there is no apparent benefit from CEA until after the first year. However if for any reasons, the perioperative morbidity and mortality is higher in asymptomatic patients (4.5% range 3% to 5.3%) no real surgical benefit is achieved in the first 5 years postoperatively. The benefit seen in ACAS trial was with low perioperative morbidity and mortality rate of 2.3%.Hence given the narrow margin benefit between the surgical and medical treatment, it is important to identify those asymptomatic patients who are at high risk for stroke and are going to benefit from CEA.

For individuals with less than 70% to 85% stenosis there is a stroke risk of less than 1.5% per year while in patients above this level the stroke risk is 2.5% per year. Nevertheless in ACAS trial the increasing risk of stroke or benefits from CEA were not related to increased stenosis in carotid artery. This is so because in ACAS trial the sample size was small and the number of outcome events were small. The reliance on Doppler scan rather than angiography precluded the ACAS to consider increased stenosis as increasing risk of stroke or any benefits from CEA. The effects of risk profiles such as hypertension, coronary artery disease, diabetes and smoking were not examined in ACAS trial.

The Veteran Affairs (VA) Cooperative Study trial reported a significant benefit in the surgical arm when TIAs was also included with stroke to constitute the outcome events. However if only stroke alone was considered as final outcome, the benefit from CEA was small but statistically non-significant. This benefit was negated if perioperative morbidity and mortality is increased. Women were not studied in VA trial.

The Mayo Asymptomatic Carotid Endarterectomy Study Group (MACE) compared the effects of CEA with medical treatment using low dose aspirin in patients with asymptomatic carotid stenosis.The trial was terminated early because of a significantly higher number of myocardial infarctions and TIAs in the surgical group which was related to the absence of aspirin use in the surgical group[5].

The Carotid Artery Stenosis with Asymptomatic Narrowing : Operation versus Aspirin (CASANOVA) study reported no benefit in the surgical group as compared with the medical group[6]. This study excluded from randomized patients those with stenosis of 90% or more.

From the above four trials it can be concluded that CEA in asymptomatic patients unequivocally reduces the incidence of ipsilateral stroke, though the absolute benefit is relatively small. Given the modest benefit of surgery for unselected patients with asymptomatic carotid artery stenosis, the CEA cannot be routinely be recommended for these patients pending reliable identification of high risk subgroups. In such cases medical management is a sensible alternative to CEA.The management must also concentrate on treatable risk factors and CEA should be done on a subset of asymptomatic patients based on age, concomitant risk factors, progression of the disease and overall medical status of the individual[7].

FACTORS FAVORING CAROTID ENDARTERECTOMY:

1. Clinical ischemia in the hemisphere or eye supplied by the stenosed artery
2. Brain infarct shown on CT or MRI in the hemisphere supplied by the stenosed artery
3. Severe stenosis (>80%)
4. Progression of stenosis over 6 months
5. No serious co-morbid conditions
6. Experienced surgeon with a low morbidity record
7. Contraindication to anti-platelet or anticoagulant therapy

FACTORS AGAINST CAROTID ENDARTERECTOMY: Sundt T et al. 7

1. Recent stroke
2. Progressive cerebral ischemia
3. Frequent TIA
4. Multiple brain infracts
5. Carotid artery bifurcation high in neck (C2 Level)
6. Thrombus in ICA
7. Severe stenosis in the contralateral artery
8. Stenosis of the intracranial carotid artery or its branches
9. Previous carotid artery surgery
10. Hypertension, CAD, CHF, DM
11. Chronic pulmonary disease
12. Smoking
13. Renal or hepatic disease

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CONGENITAL LOBAR EMPHYSEMA: PITFALLS IN DIAGNOSIS

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Introduction:

The first description of CLE was by Nelson in 1932[1]. Since then many reports followed but it still tends to be diagnosed late and after considering other diagnosis[2,3]. The occurence of breathlessness in an infant without fever or heart disease should raise the suspicion of CLE, but unfortunately most of these patients have a concomitant upper respiratory tract infection at presentation and that confuses the clinical picture[3,4]. Herein we present our clinical experience in a hospital which is referral to the North Western part of Saudi Arabia with an annual workload of 15,000 deliveries and 5,000 paediatric admissions. Our aim is to demonstrate the diagnostic difficulties we faced in the management of these patients and would attempt to prioritize the diagnostic investigations.

Clinical Material

Between July 1990 and December 1992 the diagnosis of CLE was entertained in 7 patients. Their clinical presentation, management and outcome is shown in table I. The chest X-ray (CXR) was typical for CLE in 5 patients including patient No. 3 whose CXR showed initial cystic changes. The CT scan was done for 3 patients. It confirmed the CXR diagnosis in patient No. 2 by demonstrating a hyperinflated right middle lobe, and collapse of the right lower and upper lobes. It did not add much information in case of patient No. 6 & 7 whose final diagnosis were confirmed by ventilation perfusion scan (V/Q) studies; and they did not have CLE. The V/Q studies were performed by using radiolabelled Technitium & Xenon. Bronchoscopy was undertaken for patients No. 4, 6 & 7. It did not reveal any abnormality in either of these patients and resulted in pneumothorax in patient No. 4. Two patients with CLE (No.2 & 4) were erroneously diagnosed as pneumothorax. Four patients with CLE had successful lobectomy and the 5th deteriorated very fast and expired before surgery. Lobectomy was easy in 3 patients but was a lengthy procedure in patient No. 4 because of intercurrent chest infection and adhesions. Post-operative recovery was uneventful in all cases. Histological examination of resected lobes confirmed the diagnosis of CLE in all of our patients.

Discussion:

Congenital lobar emphysema varies in its presentation and the earlier it presents the more severe are the symptoms[3]. This was evident in two of our patients (No. 2&5). The eldest case in our series was 4 months old but late presentation has been reported upto adulthood[5]. Our findings were in accord with others who found that the lobes commonly affected are the left upper, right middle and right upper lobes respectively[4,6,7]. The clinical diagnosis of CLE is difficult but typical cases do show typical CXR findings. These findings were described by Kenedy et al[8] as overexpansion of the affected lobe with or without herniation to the opposite side, compression of adjacent lobes, mediastinal shift, widening of rib spaces and flattening of the diaphragm on the affected side. These findings were epresent in 4 of our cases. The CT scan was done for the rest and it was helpful in confirming the CXR diagnosis of CLE in one patient by demonstrating overinflation of the affected lobe and collapse of the adjacent ipsilateral lobe. In the remaining 2 patients the CT scan could not differentiate between CLE and compensatory emphysema. Therefore we had to undertake V/Q studies which established the diagnosis shown by Pardes et al[9].

The CT scan is useful in revealing local cases of obstruction, especially if mediastinal tumours are suspected as a cause of CLE. Kennedy et al[8] demonstrated the value of V/Q studies not only in diagnosis of CLE but also in the long term follow up of these patients when managed conservatively. Therefore we think, like others[10,11], that if the CXR does not settle the diagnosis of CLE the second investigation should preferably be the V/Q study if it is available. Bronchoscopy was undertaken in 3 of our patients but did not help in furnishing a diagnosis and resulted in iatrogenic pneumothorax in one

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of them. It is probably helpful in the rare occasion of endobronchial mucus plug obstruction[12] and undertaking it immediately prioor to surgery might be worthwhile in such cases. Pneumothorax is commonly confused with CLE[9,12] and this confusion proved fatal in case No. 2. A careful look at the plain CXR and any evidence of the presence of bronchovascular markings weigh against the presence of pneumothorax. Also in pneumothorax the lung collapses towards the hilum while the hyperinflated lobe of CLE compresses the lobes below and above it. There is limited use of angiography in CLE and is mainly useful for cases where vascular anomalies are suspected[14]. Other conditions confused with the diagnosis of CLE are endobronchial foreign bodies, cystic adenomatoid malformation of the lung (CAM) and pulmonary sling syndrome. The latter is due to an aberrant branch of the pulmonary artery that swings below the carina to the other side compressing the main bronchus and causing emphysema of the entire lung[15]. CAM is a real diagnostic difficulty[16,17]. In this dysplastic abnormality a portion of the lung is malformed and while initially fluid filled, it eventually becomes air-filled[17]. This rsults information of numerous lung cysts of varying sizes and in contrast to CLE can affect any lobe. The CXR and CT scan are enough to diagnose CAM[17]. The diagnosis of CAM was refuted in one of our patients without resort to CT scan.

In conclusion CLE is one of the most important and treatable causes of respiratory distress in infancy and a high index of clinical suspicion is needed for its diagnosis. The plain CXR, PA and lateral view, is enough to confirm it in most of situations. The V/Q study should take precedence over all other investigations if it is available.

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HOLES IN THE HEART

Fayaz A. Shawl

Clogged arteries in and around the heart reduce the amount of oxygen and nutrient carrying blood that reaches the heart muscle. Angina--chest pain around the heart, signals the problem. For decades, doctors have successfully cleared the blockage by by-passing the arteries or opening them in to balloon angioplasty therapy. Some patients however, do not have appropriate arteries for these treatments.

The world's first mechanical Percutaneous Myocardial Revascularisation (PMR) procedure designed to treat patients with a severe form of heart disease has been performed by Dr. Fayaz A. Shawl, Director of Interventional Cardiology at Washington Advantist Hospital.

Working between heart beats, Dr. Fayaz A. Shawl threaded a miniature drill inside a Maryland man's heart (Norman Ridgeway) punched 15 tiny holes in his left ventricle in a half-hour.

During the procedure, a Catheter is threaded through the femoral artery into heart, a tiny needle, which rotates at about 1,000 - 2,000 revolution per minute, is then placed inside the Catheter and used to drill tiny holes in the heart. These holes create channels for blood to flow through the heart thus bypassing the severely clogged arteries which restrict the necessary supply of blood. This concept was derived from the heart of reptiles which circulate blood through channels rather than blood vessels.

Minutes later - still lying on the operating table, the first American to undergo the experimental drilling made a susprising statement:- He already felt relief from the excruciating chest pain and breathlessness that had left him disabled.

Ridgeway underwent bypass surgery and 13 angioplastic over the past 15 years but continued to decline until doctors had nothing left to offer - another surgery would kill him. Yet Ridgeway went home 24 hours after undergoing the experimental needle drilling, although not cured but insisting he felt better. But Shawl, who first tried his drilling technique on nine patients in India, says they are doing well-believes the relief is real.

The FDA recently approved open-heart laser surgery as a last chance-treatment for severe angina . But open heart surgery is dangerous for very ill people and some 8 percent of angina patients die during open heart laser drilling called "Transmyocardial Revascularisation. So doctors now are trying a less invasive method of burning holes, by threading a wire-like laser through an artery from the patient's groin up to the heart.

The procedure is still highly experimental, while Shawl has performed it and contends it helps patients who could not survive surgery, he says the laser wire is difficult to control and flops around as it's positioned in the heart. Good control is crucial to keep holes from boring so deep that they punch through the heart wall. The new needle - drill is much easier to control and would cost $ 20,000 far less then the $250,000 of laser treatment.

EBSTEINS ANOMALY OF LEFT AV VALVE IN A PATIENT WITH LTGA

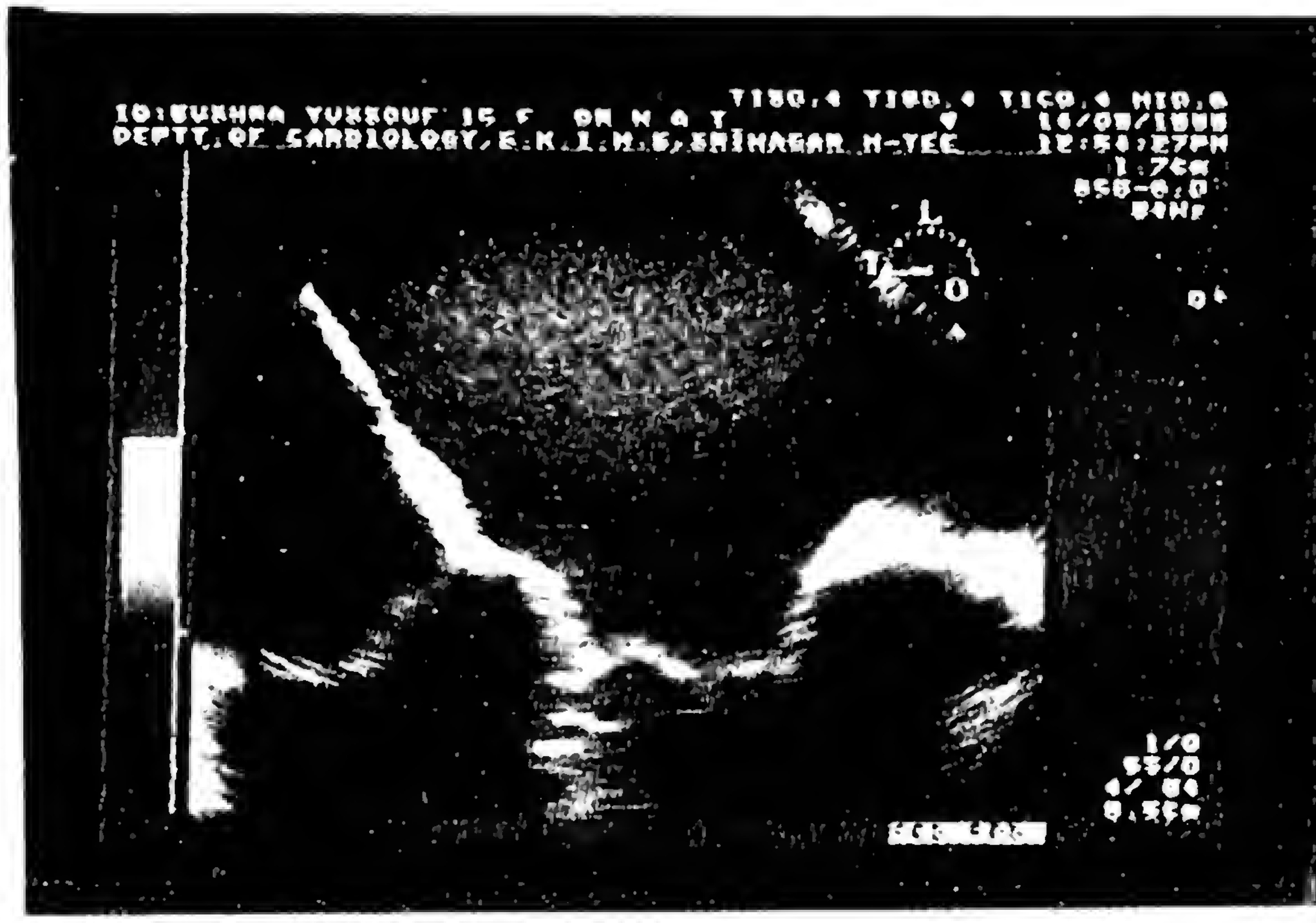

Fig. I: Transesophageal echocardiography Showing left sided Ebstein's anomaly

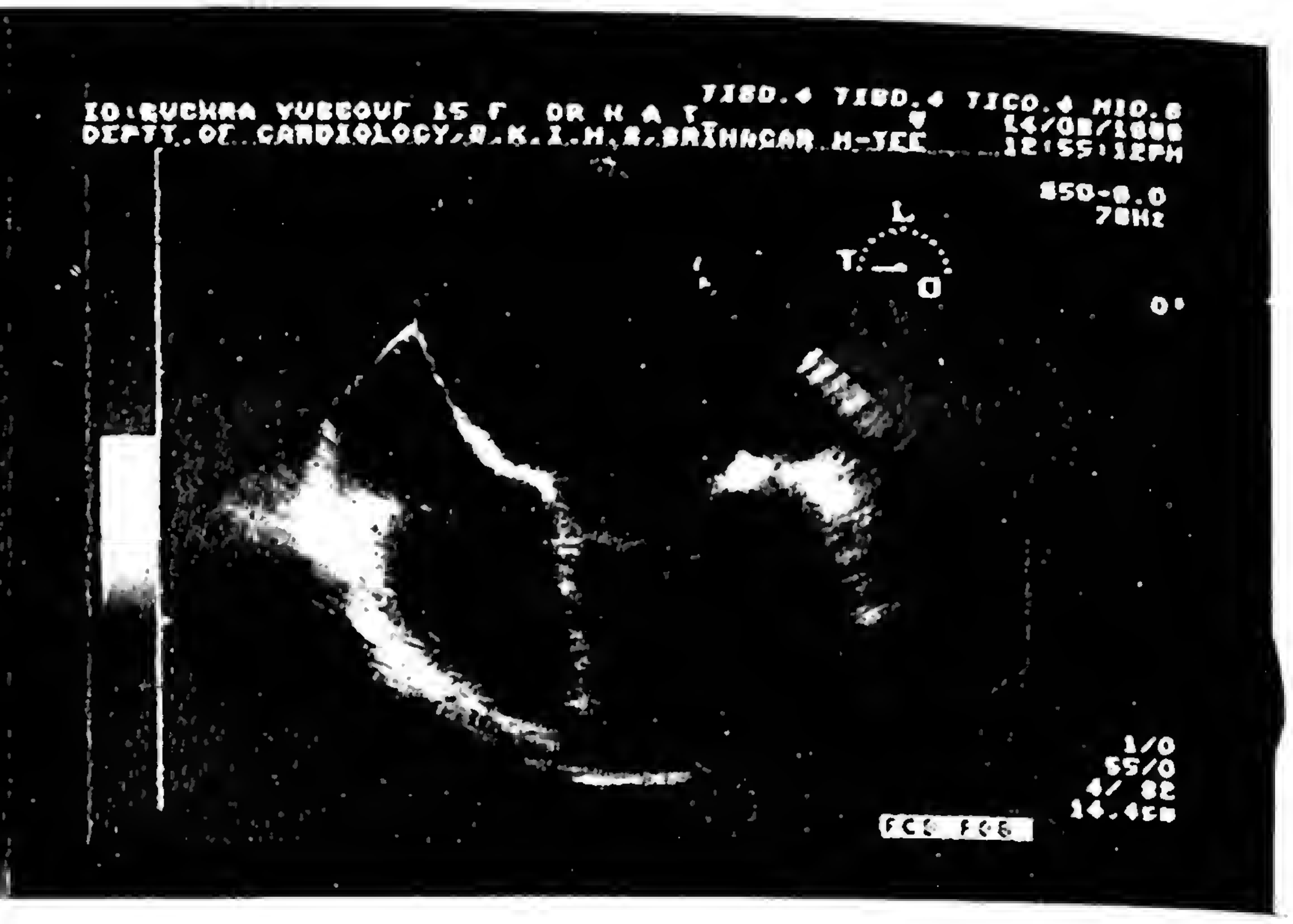

Fig. II: Transesophageal echocardiography showing displaced A.V. value with left sided Ventricle showing coarse trabeculations, features suggestive of LTGA

20 years female presented with exertional shortness of breath and palpitations (Class-II symptoms). Her CVS examination revealed cardiomegaly with apex down and out. There was a pansystolic murmur at apex with soft SI and LVS3. ECG revealed left atrial enlargement, PR prolongation, left ventricular hypertrophy, absence of Q-in 1, AVL, V5 & V6. X-ray chest showed cardiomegaly, CTR of 60% with a narrow vascular pedicle. Transesophageal echo showed LTGA with intact IVS and IAS, left sided AV valve regurgitation of moderate severity and displaced left AV valve and left atrial enlargement.

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JK-Practitioner 2000; 7(3): 236

ACCESSORY IRIS MEMBRANE

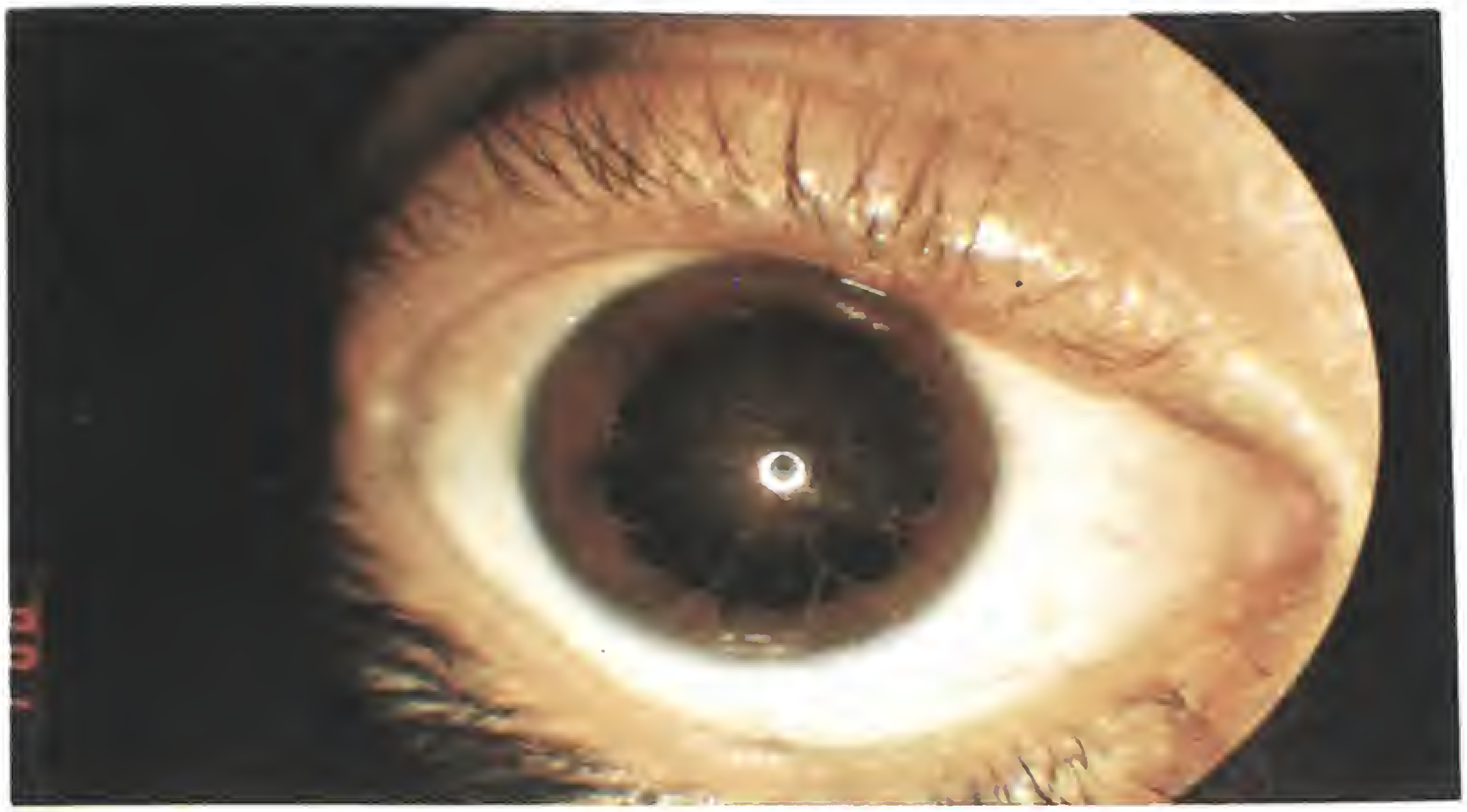

Fig. I: Accessory Iris Membrane.

A 14 year old school boy presented with gross diminution of vision in R/E since early childhood. There was no other ocular complaint and the family history was also insignificant. On examination the visual acuity in right eye was FC: 3M and in left eye it was 6/6. Retinoscopy in right eye was -11D in both vertical and horizontal meridian, but there was no improvement with glasses. In both the eyes, from the anterior aspect of the iris, buldged a normal coloured iris tissue with multiple defects and a pseudopupil in the centre. This accessory iris tissue would arise from the collarette and was not having any other attachment with the underlying normal pupillary margin or the lens. Opthalmoscopy in right eye revealed a pale disc with myopic crescent, while in left eye, it was normal. A diagnosis of bilateral accessory iris membrane with onisometropic amblyopia in right eye (due to uncorrected high myopia) was made and it was suggested that unless associated with some other pathology (like cataract or myopia), the accessory iris membrane remains asymptomatic and does not require any treatment or intervention.

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1. SIALASTIC INFANT FEEDING TUBE AS AN ALTERNATIVE TO A CONVENTIONAL VALVELESS VENTRICULO PERITONEAL SHUNT.

A 35 year old lady with severe headache & blurring of vision was admitted to our hospital with the diagnosis of Rt. Temporal lobe arachnoid cyst. In the immediate preoperative period patient had an attack of seizures and was showing a decerebrate posture. Foleys urinary catheter was placed and brain decongestant therapy in the form of Inj. Mannitol (300ml) & Inj. Lasix (20mg-IV) was started. Patient was shifted to the operation theater and general endotracheal anesthesia was induced. A right temporal free bone flap craniotomy was done, cyst was punctured and intracystic pressure was recorded to be lower than normal. In view of low intracystic pressure it was decided to place a low pressure or a valveless shunt. Since the conventional low pressure shunt was not available, we resorted to a sialastic tube used for infant feeding which was placed as a cystoperitoneal shunt.

General anesthesia was reversed and patient was shifted to recovery room in an awake state. Postoperative period was uneventful and patient was discharged from the hospital.

We believe that at places where conventional V.P. shunts are not available neurosurgeon can take the advantage of using a simple sialastic or polyvinyl chloride infant feeding tube especially during emergency situations.

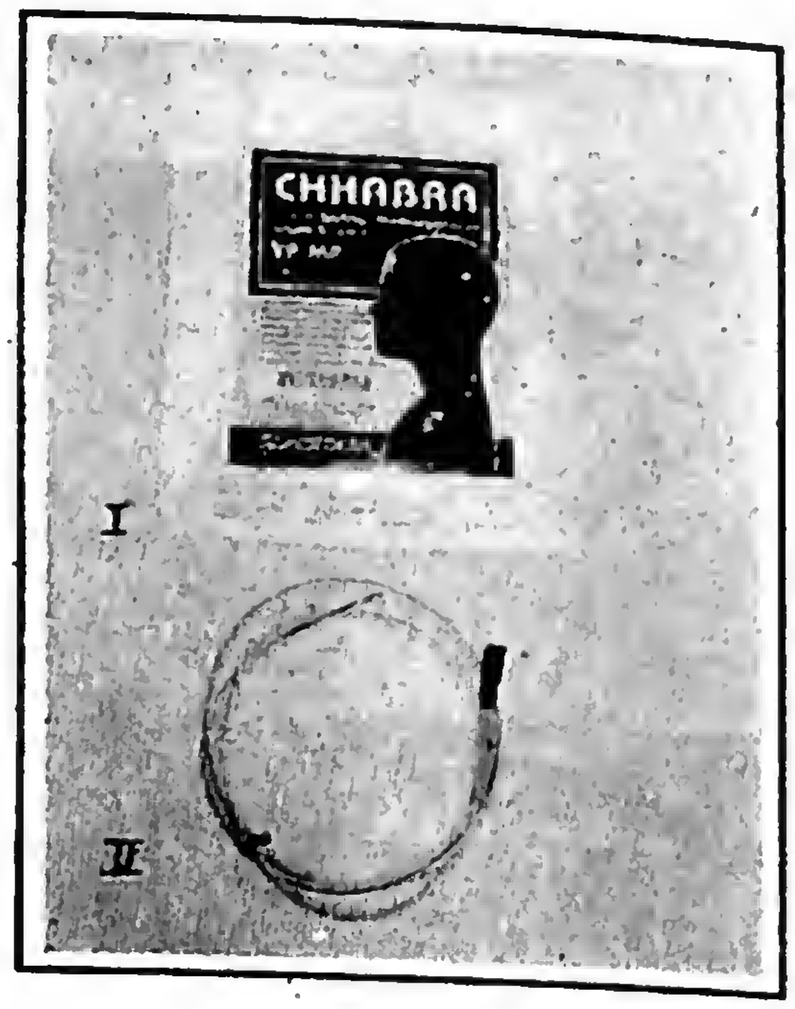

Figure.I. Medium Pressure Chhabra ventriculo peritoneal shunt.
II. Salastic infant feeding tube.

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2. USE OF 20 G HYPODERMIC NEEDLE AS INTRODUCER FOR PLACEMENT OF 26.5 & 27 G QUINKE TIP SPINAL NEEDLES.

One of the reasons incriminated for postspinal headache is using a bigger gauge spinal needle but placing a smaller gauge needle needs the services of an experienced anesthesiologist and at places like ours where there is lot of patient burden on the operation theaters it will be time consuming to place finer needles for spinal blockade, so introducers are a must for using such needles. Since introducers are not readily available, we use a 20 G hypodermic needle which is readily available with a 10ml disposable syringe and results obtained are excellent in the form of incidence of postspinal headache and time consumption for giving subarachnoid block.

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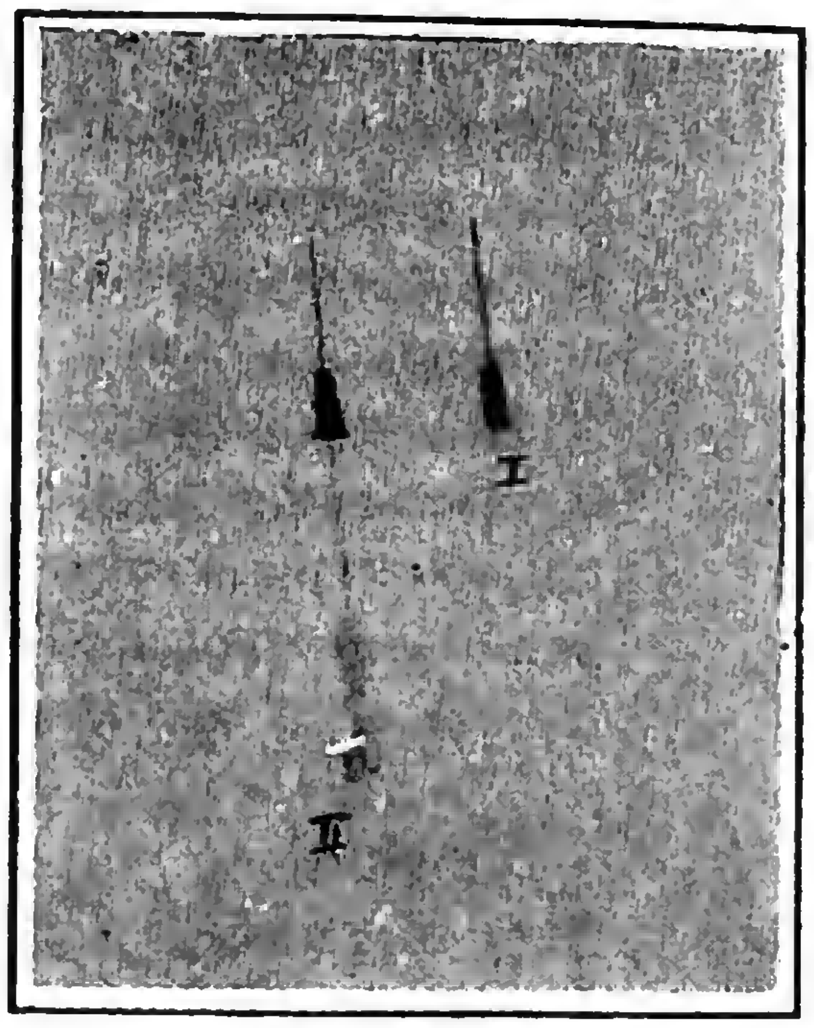

Figure.2. I. 20G Disposable Hypodermic needle.
II. 26 G Quinketip needle alongwith Stilette passing through 20G disposable Hypodermic needle.

LETTER FROM NEW YORK

CONTRIBUTIONS OF THE GOVERNMENT MEDICAL COLLEGE (GMC) ALUMNI AT THE ANNUAL SESSION OF ACP-ASIM IN PHILADELPHIA, USA FROM APRIL 13-16, 2000

ACP-ASIM is the largest medical specialty organization in the world, with over 120,000 members all over the world. From these members, 372 have been awarded Mastership in the college. This award is bestowed in recognition of the personal character, position of honor and influence, eminence in practice or in medical research, or other attainments in science or in the art of Medicine. For the year 2000, Dr. Mohammad Sultan Khuroo was awarded mastership, which he received during the annual convention in Philadelphia. This convention was attended by over six thousand physicians from all parts of the world. The other GMC alumni who made contributions at this meeting were:

- Dr Riyaz Bashir, who represented the trainees in Medicine from the state of Massachusetts.
- Dr. Tanveer Mir, Governor of Region III of the New York State ACP-ASIM chapter. She also made a presentation at the International Medical Graduate Forum.
- Dr. Muzaffar Ahmad who gave two sessions on the management of bronchial asthma.
- Dr. Prediman K. Shah, moderated a panel discussion on the approach to unstable angina.
- Dr. Faroque A. Khan, who participated in the Regents' (governing body of ACP-ASIM) meeting and directed two workships on mechanical ventilation.

Fully Dressed for the occasion. Faroque A. Khan & M.S. Khuroo in Philadealphia, April 2000

The staff, faculty and students of GMC deserve congratulations on the accomplishments of these GMC alumni.

The ACP-ASIM has now made available an international poster competition. Students and house physicians-in-training are invited to submit their work for next year's annual meeting to be held in Atlanta, Georgia from March 29th to April 1st, 2001. Further information may be obtained from:

Ms. Lisa Landrum-International Affairs
American College of Physicans-American Society of Internal Medicine
190 North Independence Mall West
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◆ **Acadima 2000. A Medical Conference Planned by the Indian Medical Association (IMA) in Delhi from 20th - 22nd October 2000.**
For Registration and details contact. Room No. 220, I.M.A. House, Indraprastha Marg, New Delhi - 110002. Tel +91-11-3359177, 3319009, 3318819, 3318058, 33186880 Fax +91-11-3359178. 3316270 Telegram "INMEDICI" New Delhi.

E-mail inmedici@ndb.vsnl.net.in
Internet: http://www.ima1928.com.

◆ **The 6th Asian Pacific American gastroenterological Conference and the 41st. Annual Conference of Indian Society of Gastroenterology will be held in New Delhi on November 19-25,2000.**
For details please visit website www.isgcon2000.com or contact Dr. Rakesh K. Tondon, Organizing Secretary, Deptt. of Gastroenterology, All India Institute of Medical Sciences, New Delhi - 110029.

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isgcon2000@hotmail.com.

◆ **IMA Kashmir Banch Organising Ist Annual Conference in 2nd week of September 2000 at Srinagar**
for Specialists and Practitioners etc. for details contact Mir Nazir Ahmad Secretary, Mir Manzil, Hyderpora, Bye Pass, Srinagar.

◆ **Second World Congress on Vaccines and Immunization, Liege, Belgium 29 August-3 September 2000**
Information: Edouard Kurstak, ICWO-Univerrsity of Montreal, QC H9H 3G4, Canada.

◆ **Postgraduate Clinics in Gastroenterology 2000 (Focus on 'Investigative Modalities in Gastroenterology'), Lucknow, Uttar Pradesh 1-3 September 2000.**
Information: Rakesh Aggarwal, Department of Gastroenterology, SGPGI, Lucknow 226014, Uttar Pradesh, India.

◆ **International Training Course on Frontiers in Cancer Genetics sponsored by UNESCO-ISRO (International Cell Research Organization), New Delhi, India 14-28 September 2000.**
Informaltion: K. Kucheria, Department of Anatomy, All India Institute of Medical Sciences, New Delhi 110029, India.

◆ **Tenth National Conference of Indian Association of Surgical Gastroenterology, Patna, Bihar 15-17 September 2000.**
Information: C. Khandelwal, Department of G.I. Surgery, Indira Gandhi Institute of Medical Sciences, Patna 800014, Bihar, India

◆ **World Stroke Congress, Melbourne, Australia 25-29 November 2000**
Information: ICMS Pvt. Ltd., 84 Queesbridge Road, South Bank, Victoria, Australia 3006

◆ **International Seminar on Haemoglobinopathies: South Asia-Problems and Prevention, Calcutta, West Bengal,. India 27-29 December 2000**
Information: Madhusnata De, Organizing Secretary, Vivekananda Institute of Medical Sciences, 99 Sarat Bose Road, Calcutta 700026, West Bengal, India.

◆ **Third International Workshop on Advanced Therapeutic Endoscopy and National Conference of Society of Gastrointestinal Endoscopy of India, Mumbai, Maharashtra 3-6 February 2001.**
Information: Amit Maydeo, Digestive Disease Centre, Bhatia General Hospital, Tardeo, Tardeo Road, Mumbai 400007, Maharashtra, India.

DR P.N. BERRY'S EDUCATIONAL TRUST SCHOLARSHIP SCHEME FOR INDIA

The Committee of Selection for India invites applications from nurses, physiotherapists and doctors for The Dr. P.N Berry Scholarships for India. These scholarship are tenable for 4 months of trining at medical institutions in India. The upper age limit (on 1 October) is 40 years. Only citizens of India who have lived here for at least 5 years are eligible.

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ACE INHIBITORS AFTER MYOCARDIAL INFARCTION*

The brief description of the relevant trials clearly indicate that ACE inhibitors have a potential to prevent major ischemic events and therefore alter the natural history of atherosclerotic disease. One study which was not covered in the pervious issue is SOLVD[15].(Studies of left venicular dysfunction). SOLVD prevention study enrolled patients with $EF < 35\%$ without heart failure and SOLVD treatment study enrolled those wih $EF<35\%$ but with HF. It was seen that risk for acute infarction was significantly reduced over a 40 month period. When the data of SOLVD, SAVE, AIRE and TRACE studies is Pooled a 21% risk reduction ($p<0.002$) for MI is observed. Other Ischemic end points such as hospitalization for unstable angina, is also significantly reduced. Patients in SOLVD and SAVE trials had low ejection fraction in whom renin and angiotensin levels are expected to be higher, therefore data cannot be extrapolated to patients with normal EF. However the relationship between the degree of LV dysfunction and reduction in MI was weak ($p=0.04$) therefore the mechanism of risk reduction in patients without LV dysfunction deserves futher exploration.

It is also clear that the beneficial effects such as MI Reduction takes a logner period for becoming clinically evident suggesting that it cannot be solely due to its hemodynamic effects which are achieved very quickly. There observtions suggest that ACE inhibitors might be working through multiple mechanisms including the prevention of coronary atherosclerosis progression and or/stabilization of atherosclerotic plagues.

It can be therefore concluded that ACE inhibutors should be started during the first day following AMI in most patients with careful monitoring of BP and hemodynamic status. If echo shows reduced EF, the therapy should be continued indefinetely while in others who have no objective or subjective evidence of LV dysfunction, treatment can be stopped.

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JK-Practitioner 2000; 7(4):

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ANGIOGENESIS: BASIC CONSIDERATIONS AND APPLIED RESULTS

Riyaz Bashir M.D.; Peter R. Vale, M.D.; Jeffrey M. Isner, M.D.; Douglas W. Losordo, M.D.

Mechanism of efficacy, safety concerns and early results

Coronary and peripheral atherosclerotic diseases affect more than 15 million patients in United States alone. Over last three decades significant progress has been made in the management of these patients using medical, surgical and percutaneous therapies. However there remains a significant population of patients who are not optimal candidates for surgical or percutaneous revascularization. These patients continue to suffer from the debilitating symptoms of their disease and remain at risk for myocardial events, limb loss or death. It was this clinical need, coupled with the advances in the understanding of angiogenesis that has led to efforts to develop angiogenic therapies for patients with peripheral and myocardial ischemia. In general these conditions are characterized by local hypovascularity and the approach to treatment is focussed on stimulating neovascularization, i.e., therapeutic angiogenesis.

Angiogenesis is defined as formation of new blood vessel from pre-existing vessels by the process of cellular outgrowth. It differs from vasculogenesis , which is typically considered an embryonic phenomenon in which new blood vessels are formed from committed stem cells. Angiogenesis can be both physiological and pathological, the former being formation of new vessels after embryonic life in processes such as wound healing and the female reproductive cycle. Examples of pathological processes involving angiogenesis include tumor growth, rheumatoid arthritis and diabetic retinopathy.

It was the work of Dr. Judah Folkman and his colleagues that identified the dependence of tumor growth on local angiogenesis and suggested that certain angiogenic growth factors were responsible for this process. Therapy to limit or reverse tumor growth using inhibitors of angiogenic growth factors is now under investigation and is showing promise[1].

Conversely, the treatment of pathological ischemia resulting from vascular occulusive diseases would require that the process of angiogenesis be augmented in the hypoperfused myocardial and skeletal muscle tissues. Attempts to augment local tissue perfusion in patients who are not amenable to conventional surgical or percutaneous revascularization have included:

1. Use of angiogenic growth factors
2. Transmyocardial laser
3. Low intensity electrical stimulation.

Angiogenic Growth Factors

The majority of the work in therapeutic angiogenesis has been done using various angiogenic growth factors. There are numerous angiogenic growth factors which have been investigated as potential agents for therapeutic angiogenesis:

Vascular endothelial growth factor*	VEGF
Basic fibroblast growth factor	bFGF/FGF2
Acidic fibroblast growth factor	aFGF/FGF1
Fibroblast growth factor 4	FGF$
Fibroblast growth factor 5	FGF%
Angiopoietin 1*	Ang 1.
Angiopoietin 2*	Ang 2.
Heparin-binding epidermal growth factor	HB-EGF
Placental growth factor*	PIGF
Scatter-factor hepatocyte growth factor	HGF
Insulinlike growth factor	IGF
Platelet derived growth factor	PDGF
Transforming growth factor B	TGF-B

** Specific for endothelial cells.*

Most clinical studies to date have focused on VEGF and FGF.

Mechanism of angiogenesis

The full paradigm for angiogenesis[2] has been suggested to begin with "activation" of ECs within a parent vessel, followed by disruption of the basement membrane, and subsequent migration of ECs into the interstitial space, possibly in the direction of an ischemic

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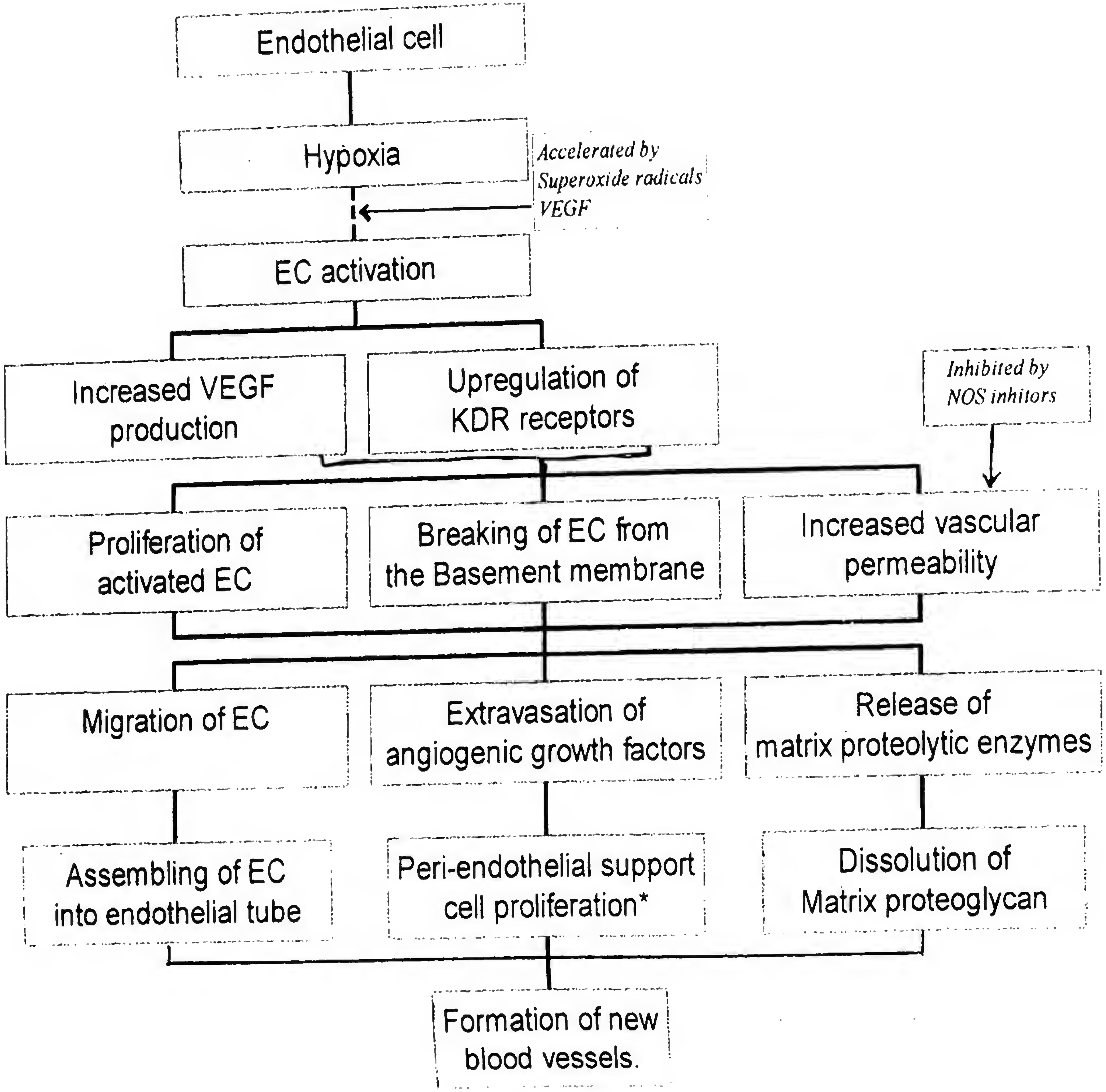
Mechanism of Angiogenesis


Endothelial cell
Hypoxia
Accelerated by
Superoxide radicals
VEGF
EC activation
Increased VEGF production
Upregulation of KDR receptors
Inhibited by
NOS inhitors
Proliferation of activated EC
Breaking of EC from the Basement membrane
Increased vascular permeability
Migration of EC
Extravasation of angiogenic growth factors
Release of matrix proteolytic enzymes
Assembling of EC into endothelial tube
Peri-endothelial support cell proliferation*
Dissolution of Matrix proteoglycan
Formation of new blood vessels.

stimulus. Concomitant and/or subsequent EC proliferation, intracellular-vacuolar lumen formation, pericyte "capping", and production of a basement membrane complete the developmental sequence. (Fig. 1)

During angiogenesis, migration precedes proliferation by approximately 24 hrs.[3] This principle was best demonstrated in classic experiments performed by Sholley et al using a model of inflammation-induced angiogenesis of the rat cornea, in which initiation of vascular sprouting was shown to occur in the absence of EC proliferation which was suppressed by X-irradiation prior to application of the inflammatory stimulus[4]. In irradiated corneas displaying no cellular proliferation, vascular sprouting at 2 days was similar to that seen in contralateral shielded corneas. While neovascular growth was subsequently blunted and ultimately ceased by 4 to 7 days, these experiments documented the critical if not exclusive roles of migration and redistribution of pre-existing ECs in the commencement of neovascularization. Similar implications resulted from work by Nicosia et al;[5] fibronectin was shown to promote, in a dose-dependent fashion, the elongation of microvessels which sprout from explants of rat aorta placed in serum-free collagen gel - despite the fact that neither DNA synthesis nor mitotic activity was increased in comparsion to fibronectin-negative gels. Fibronectin was therefore inferred to promote engiogenesis in vitro by migratory recruitment of pre-existing ECs. Subsequent studies have established the critical role played by plasmin and other proteases in promoting migration through pre-existing matrix[6, 2]

In contrast to these in vivo inflammatory and in vitro organ culture models, angiogenesis which develops in response to experimental vascular obstruction, i.e. collateral vessel development, has been shown by several previous investigators to involve proliferation of not only ECs, but SMCs as well. Several important principles were elucidated by these studies.

First, evidence of EC proliferation is nearly absent in normal arteries [8, 9] a finding which is consistent with an estimated EC turnover time of "thousands of days" in quiescent microvasculature[10]. Even a relatively low percent of EC proliferation observed in response to arterial occlusion or exogenous growth factors may therefore represent considerable enhancement of EC proliferative activity, and, when considered in relation to a denominator of thousands of ECs, is clearly sufficient to provide the basis for new blood vessel formation. Second, EC proliferation which contributes to naturally occuring collateral development in the setting of vascular occlusion varies from 2.6% to 3.5% in the canine coronary;[9-11] from 5 to 6% in the rodent renal vasculature; Ilich 1979 and is < 1% in swine coronaries.[12] The contrasting rates of EC proliferation between the canine and swine coronary circulations are in parallel with the relative propensity for natural collateral artery development in these two species. Third, proliferation of SMCs, the additional requisite cell type for the formation of larger blood vessels, is an implicit component of angiogenesis, regardless of animal species or circulatory site.[13] Fourth, proliferative activity - for SMCs as well as ECs - is highest at the level of the smallest-diameter collateral vessels, the so-called midzone collateral segments.[9,11,14,15] Fifth, while evidence of EC and SMC proliferation alone does not necessarily distingusih new vessels, adjunctive data regarding increased capillary density[16,17] support the notion that proliferative activity does in fact reflect true angiogenesis.

Post-natal Vasculogenesis

In the embryonic yolk sac, vasculogenesis involves growth and fusion of multiple blood islands which ultimately give rise to yolk sac capillary network;[18] after the onset of blood circulation, this network differentiates into an arteriovenous vascular system[19]. The integral relationship between the elements which circulate in the vascular system-the blood cells- and the cells which are principally responsible for the vessels themselves - endothelial cells (ECs) - is implied by the composition of the embryonic blood islands. The cells destined to generate hematopoietic cells are situated in the center of the blood island and are termed hematopoietic stem cells (HSCs). Endothelial progenitor cells (EPCs), or angioblasts, are located at the periphery of the blood islands. In addition to this spatial association, HSCs and EPCs share certain antigenic determinants, including Flk-1, Tie-2, Sca-1 and CD-34. These progenitor cells have consequently been considered to derive from a common precursor, putatively termed a hamangioblast.[20,22]

Postnatal neovascularization has been previously considered to result exclusively from the proliferation, migration and remodelling of fully differentiated ECs derived from preexisting blood vessels from endothelial progenitor cells (EPCs) or angioblasts - i.e. vasculogenesis has been considered restricted to embryogenesis.[19,23]

Our laboratory reasoned, however, that the use of HSCs derived from peripheral blood in lieu of bone marrow to provide sustained hematopoietic recovery constituted inferential evidence for circulating stem cells. Circulating CD34 antigen-positive EPCs were recently isolated from adult species; once adherent, these cells were shown to differentiate along an endothelial cell lineage in vitro[24]. (see preliminary data) Heterologous, homologous or autologous EPCs adminstered systemically to animals with operatively induced hindlimb ischemia were found to incorporate into foci of neovascularization in ischemic muscles of the affected hindlimb. These findings, together with other recent studies[25, 26] have been interpreted as evidence for postnatal "vasculogenesis"[19, 23]

Many of these steps are controlled by paracrine signals from aniogenic growth factors such as VEGF and angiopoietins 1&2[27] These factors or cytokines bind to and modulate the activity of transmembrane receptor tyrosine kinases (RTKs). VEGF binds to two such receptors on endothelial cells, which are VEGFR-1 also called Flt 1 and VEGFR-2 also called KDR or Flk 1. The former receptor generates signals that organize the assembly of endothelial cells into tubes and functional vessels while the later is responsible for endothelial cells proliferation and migration. Hypoxia induces the formation of VEGF receptors.[28] Angiopoietin 1 & 2 bind to another RTKs called Tie 2, producing two opposing effect on this process. Basic FGF is believed to bind to independent RTKs on the cell surface, however it is not endothelial cell specific and is a potent mitogen for a variety of other cell types including smooth muscle cells.[21,19]

Vascular Endothelial Growth Factor

VEGF is a secreted glycoprotein, which has been identified in four homodemeric forms arising from alternative splicing of mRNA from single gene. Each molecule contains 121, 165, 189 or 206 amino-acids and are capable of binding heparin or cell surface heparan sulphate proteoglycans. All forms are mitogenic towards vascular endothelial cells and increase vascular permeability of blood vessels. VEGF 165 is the predominant form.

VEGF can be adminstered either as a recombinant protein or as a gene encoding for this peptide.

A. Gene Transfer of VEGF

A series of investigations in animals and humans have demonstrated the feasibility of transferring naked plasmid DNA encoding VEGF. Even though evidence of transfection is noted in less than one percent of endothelial cells, the secreted gene product has significant biological effects. Several routes of administration have been studied.

Arterial VEGF gene transfer: In studies of arterial gene transfer VEGF gene was delivered as naked DNA to the internal iliac artery in rabbits with hind limb ischemia. The transfer was faciliated by applying solutions of pure plasmid DNA to the hydrogel polymer coating of a standard angioplasty balloon. The balloon was inflated and DNA was transferred to the arterial wall. Analysis of the transfected internal iliac artery using reverse transcription PCR, confirming the presence of VEGF mRNA after gene transfer. Gene expression persisted for 2-4 weeks after transient transfection with naked DNA and evidence for new collateral vessels was provided by serial angiography and by increased capillary density at necropsy. The ischemic limb also showed improved hemodynamics in the form of increased calf blood pressure ratio (CBR) and increased distal maximum flow velocity in response to papaverine using a doppler flow wire.

Clinical Studies:

Eight patients with critical limb ischemia (pain at rest or non-healing ulcers), who were not candidates for surgical revascularization, were enrolled. The VEGF 165 gene was administered into the artery in ascending doses in a Phase I study. The transfer site was examined by IVUS prior to delivery of the gene, in order to exclude evidence of atherosclerotic plaque or intimal thickening. Three patients who had nocturnal rest pain only received a 1 mg dose of VEGF 165. All three patients became free of rest pain at three months. MRA and contrast angiography demonstrated increased distal flow. Prior studies have suggested that the size of collateral vessels derived as a result of angiogenic gene therapy will be below the limit of detection of contrast angiography, and contrast angiography failed to demonstrate new collateral vessels in these patients. DNA labelling studies in swine and canine models of myocardial ischemia have established that increases in flow resulted from development of collaterals that are less than 180 um in diameter, below the sensitivity of standard contrast angiography.

One patient who received 2 mg dose of plasmid DNA did show direct angiographic evidence of new collateral vessels.

Intramuscular Gene Therapy: Studies from our laboratory have shown that transfection efficiency was increased to 5% to 10% by intramuscular delivery of plasmid DNA into the ischemic tissue. Hence we studied nine patients with critical limb ischemia, most of whom have been advised to undergo amputation. Each patient was injected with 2 mgs of plasmid DNA at four sites into the muscles of the ischemic limb. The same dose was repeated after four weeks.

The increase in VEGF level in the serum was documented by enzyme linked immunosorbant assay (ELISA). The mean ankle-brachial index was increased from 0.33 at baseline to 0.48, 12 weeks later. The newly developed collaterals were seen both on MRA and contrast angiography. Three patients with rest alone had complete relief of symptoms, while four of the seven patients with ischemic ulcers completely healed. To date more than 75 patients with critical limb ischemia have been treated with this form of therapy. Virtually all patients with rest pain alone have been treated successfully and have been spared amputation. About half of the patients greater than 50 years age have healed their ischemic ulcers with this therapy. We have also observed that outcome are better in younger patients.[30]

A similar form of therapy was used in 11 patients with Buerger's disease, nine of which were successfully treated. These patients had resolution of nocturnal rest pain and healing of ulcers. The ankle-brachial index increased by greater than 0.1 and newly formed collateral vessels were seen on MRA and serial contrast angiography. Two of these patients needed below knee amputation because of advanced gangrene at the time of treatment initiation, although the level of amputation was lowered in both patients.[31]

Treatment has been generally well tolerated. Adverse effects have been limited to transient ankle or calf edema, which responded well to diuretics. This has been attributed to the increased vascular permeability due to VEGF.

Myocardial gene therapy : Based on the results of the Phase I trial in patients with peripheral vascular disease, we also initiated a Phase I clinical study to assess the safety and efficacy of this therapy in patients with symptomatic coronary artery disease who were not candidates for conventional forms of revascularization.

To date 39 patients, aged 53 to 71 years have been enrolled in this study. All of these patients had class 3 or 4 exertional angina refractory to maximum medical therapy and had a reversible defect on SPECT-sestamibi myocardial perfusion imaging and by electromechanical mapping of the left ventricle. All patients had multi-vessel coronary disease that was not amenable to percutaneous or surgical revascularization. The plasmid DNA encoding VEGF 165 or VEGF-2/VEGF-C was injected directly into the ischemic myocardium by a mini left anterior thoracotomy or via a modified electro-mechanical mapping catheter. Three doses of VEGF165 were used (125 ug, 250 ug and 500 ug) to treat a total of 30 patients and this was used as a sole therapy. Gene expression was documented by the transient increase in serum levels of VEGF monitered by ELISA. Patients tolerated this therapy well and side effects were limited to unifocal PVCs. All patients had significant reduction in angina (S.I nitroglycerine used decreased from 59.3 to 2.9 tablets a week). This effect was usually seen within 21 days of gene therapy. Objective evidence of reduced ischemia was documented in 29/30 patients [32] both by SPECT-sestamibi scan as well as LV electromechanical mapping. The major advantage of this study is that it used this form of therapy as a sole therapy as opposed to most of the other clinical studies which have used the growth factors in combination with CABG.[33]

This early experience leaves several issues unresolved. Optimizing the anatomic site, number and dose of intramyocardial injection of a placebo group and clinical testing of alternative dosing regimens, including multiple treatments, will be addressed with a catheter based system for a reliable percutaneous myocardial gene delivery. This is currently in the early phases of investigation with 3 patients enrolled in a randomized, placebo controlled study of VEGF-2/VEGF-C administered using the Biosense mapping catheter that has been modified to allow injection of plasmid DNA solution into the endocardial surface of the beating heart via a femoral artery approach.

The use of adenoviral vector expressing VEGF 121 was reported to significantly to improve myocardial perfusion and function in a swine model of myocardial ischemia. This group documented myocardial perfusion and function by SPECT-sestamibi and by echocardiography during rest and stress. Currently this form of therapy is being tested in humans, so far 7 patients have received direct myocardial injection into the region of ischemic myocardium. No adverse effect of this therapy has been noted to date.[34]

B. Recombinant Human VEGF (rh VEGF)

The evidence that VEGF stimulates angiogenesis first was developed in experiments performed in a rabbit model of unilateral hind limb ischemia. Our group showed that doses of 500 to 1000 micrograms of rh VEGF produced a statistically significant augmentation of angiographically visible collateral vessels and histologically identifiable capillaries. This also resulted in improved hemodynamics in the VEGF treated ischemic limb as compared with the control. Comparable results were obtained in another series of experiments in the same model, by using intramuscular rh VEGF once daily for 10 days.

In similar pig experiments using arterial construction to create area of myocardial ischemia, recombinant VEGF increased myocardial blood flow. Banai et al reported similar results in the dog experiments using intracoronary VEGF.

Clincial Studies

Henry et al reported the early results from VIVA trial, in which effect of intracoronary followed by intravenous rhVEGF was evaluated in more than 140 patients. This was a double blind placebo controlled trial of patients with viable myocardium who were not optimal candidates for percutaneous or surgical revascularization. The doses that were used were 17 and 50 ng/kg/min on days 0, 3, 6,

& 9. Doses were limited by hypertension which developed at higher doses in an earlier dose-ranging study. The study showed that there was significant decrease in angina class in both VEGF groups as compared to placebo, however exercise treadmill time and SPECT-sestambi scan did not show any significant change. An interesting finding was that two patients in palcebo group were diagnosed to have tumours after enrollment in this study. Angiographic data is not yet available. *So far in myocardial ischemia the intramuscular rhVEGF has been used in two patients without any complications, the follow up results are awaited.[35]

Fibroblast Growth Factor (FGF)

FGF is actually a family of nine factors namely basic FGF, acidic FGF, FGF3-9.

Basic FGF is an 18 kD single chain peptide of 154 Amino-acids with both angiogenic and mitogenic potential. Acidic FGF is a 16 kD cationic polypeptide chain made up of 140 amino-acids and possesses a 55% sequence homology with bFGF. However the one that is predominantly lacking a signal peptide sequence i.e it remains sequestrated in cells that produce them. Extracellular release of FGF is caused by cell death or damage. These growth factors have strong affinity for heparin and heparin like substances mainly heparan sulphate.[36]

A series of animal experiments have demonstrated that FGF improves myocardial perfusion and function in both acute and chronic ischemia. This improvement was as a result of angiographically documented and histologically identifiable sprouting of capillary network from the original coronary vessels. After a reasonable exclusion of the tumor proliferating action of these growth factors, clinical studies have been started.

Clinical Studies: The three major ongoing clinical studies are as follows:

a. Intracoronary rFGF-2 was delivered as a single 20 min infusion divided between two major sources of coronary blood supplied in patients with non revascularizable coronary artery disease. In this open labeled, dose escalation multi-center trial there was a statistically significant decrease in angina class (2.6+0.7 to 1.2+0.8), increase in exercise tolerance (8.5+2.6 min to 10.0 + 2.5 mins) and improved regional LV function and perfusion by MRI. However there was no improvement noted in the SPECT sestamibi scan. The adverse effects that were noted include hypotension and transient renal dysfunction. There were 3 deaths and 4 myocardial infarctions reported so far on the followup.[37]

b. Perivascular bFGF, in patients undergoing CABG with viable and ischemic but non-graftable myocardial territory, was implanted in the subepicardial fat along the distribution of ungraftable vessels. In this randomized, double blinded, palcebo controlled study 10 heparin alginate microcapsules containing 10 or 100 micrograms of bFGF or placebo were used. It was reported to be well tolerated with no serious adverse effects. However in this group two patients died intraoperatively (1 control and 1 100 ugmbFGF group) and one patient had a periop. MI (10 ugmbFGF group). The preliminary data suggested improvement in angina, myocardial perfusion and regional function in the 100 ugm bFGF group.[37] Comparable results were reported by the same group in another study of eight patients using similar technique of administration.[38]

c. Intramyocardial rhFGF was used in conjection with CABG in patients with additional peripheral stenosis of the IMA grafted LAD. In this randomized double-blinded, palcebo controlled study 40 patients were enrolled (20 in FGF group and 20 in palcebo group). A 12 week follow up angiography revealed that all the patients in FGF group had an increased contrast uptake (sprouting capillary network) at the site of growth factor injection. This was noted to revascularize the vessel beyond the site of peripheral stenosis. No such contrast uptake was noted in the palcebo group that was injected with physiological saline. These findings were analyzed and supported by quantitative gray value analysis of contrast medium accumulation.[39]

These early results with FGF though encouraging are mostly seen in patients who are surgically revascularized at the same time, which makes it difficult to analyse end points like decrease in angina or improvement in myocardial perfusion scans.

Some of the animal studies have shown that intrapericardial injection of bFGF leads to angiogenesis in chronic myocardial ischemia model.

Other Growth Factors

Some of the other growth factors that have shown beneficial results in animal experiments include angiopoietin 1, human hepatocyte growth factor, acidic FGF. However there are no clinical trials reported so far.

Combination of Growth Factor

Several studies both in vitro and in vivo have demonstrated that various combinations of these growth factors have a synergistic effect on the process of angiogenesis. Asahara et al from our lab demonstrated a synergistic effect of rhFGF and rhVEGF in a rabbit model of unilateral hind limb ischemia. There was a statistically significant increase in calf blood pressure ratio, luminal diameter of the stem collaterals, number of opacified collateral, stem artery diameter and capillary density in VEGF+bFGF group as compared with VEGF and bFGF alone. The fundamental basis for the synergistic effect of VEGF and bFGF remains to be elucidated. Following are a few postulated hypothesis: VEGF is endothelial cell specific while as bFGF acts on a variety of other cell types including smooth muscle cells. It might be the combination of EC and SMC stimulation that results in enhanced angiogenesis. VEGF and bFGF act in different receptor systems. It may be that simultaneous stimulation of both the systems will be able to produce amplification of the endothelial cell response. Park et al have recently proposed another possible mechanism. They demonstrated that PIGF poteniates VEGF induced EC growth in vitro and Evan's blue dye extravasation in vivo. While PIGF binds with Flt-1, it doesn't bind KDR receptors which accounts for most of the bioactivity of VEGF. These authors suggest that interaction of PIGF and Flt-1 leads to release of VEGF from Flt-1 and increase its availability to a more relevant KDR receptors. Whether a similar mechanism exists for VEGF and bFGF remains to be investigated.

Other Methods of Inducing Angiogenesis

Recently significant interest has been generated in the mechanisms by which Transmyocardial laser revascularization reduces anginal symptoms in patients, with non-revascularization coronary artery disease. A series of experiments has revealed that it is not the long term channel patency but it is angiogenesis induced by TMR or PMR that is responsible for improved myocardial perfusion. Victor Chu reported TMR in the ischemic zone of myocardium lead statistically significant increase in the levels of TGF-beta, bFGF and VEGF. They also noted significant increase in vascular density in the laser irradiated territory (p=0.001 (Chu V. et al. Transmyocardial Laser Revascularization induced angiogenic response. JACC 1999 Feb, 342 A). Similar findings were also noted on autopsy of two patients who died after having had this form of therapy (Virmani R. Pathology of Angiogenesis. Accel 1999, : 31(3) March.

A novel method of inducing angiogenesis and increasing local VEGF levels was recently reported by using low intensity (below the contraction threshold) electrical stimulation of skeletal muscle in the rabbit's ischemic hind limb[40].

Safety Concerns

1. Tumour growth
2. Retinopathy
4. Increased vascular permeability of plaque. Hemorrhage within the plaque.
5. Anemia and Thrombocytopenia
6. Neointimal proliferation
7. Angiomas.

Angiogenesis and Risk of Cancer

Many angiogenic factors are known to be involved in tumor growth secondary to enhancing angiogenesis which is vital for growth of most tumors, particularly solid tumors. Hence, in theory, angiogenic growth factors may lead to development of tumors and they may be too small to be recognized. Even so, there is no evidence so far that this can occur. It was very interesting to note in VIVA Trial that there was a greater incidence of tumors in palcebo group than in the VEGF group. This exemplifies the fact that the age group receiving such therapy will develop some unrelated tumors. Neverthless, we must be vigilant about the possibility of cancer in patients treated with these angiogenic growth factor.

Risk of Retinopathy

It is theoretically possible that overgrowth of vessels in the retina may either induce diabetic retinopathy or worsen the existing pathology leading to loss of vision. To date, this adverse effect of therapeutic angiogenesis has not been observed. As reported by Peter Vale at AHA's annual meeting in 1998, the local delivery of naked plasmid DNA encoding for VEGF did not effect the visual acuity or fundoscopic findings in 53 patients, 32% of which were diabetic, 40% of whom already had evidence of diabetic retinopathy. As trials include larger numbers of patients, higher doses of growth factors and alternative delivery methods, we must respect the potential of this therapy to do harm.

Interstitial Edema

Angiogenic growth factors, especially VEGF which is known to increase vascular permeability, has been reported to cause local edema which manifest as pedal edema in patients treated with VEGF for critical limb ischemia. This is known to respond well to treatment with diuretics.

Hypotension

The recombinant growth factors have been noted to produce hypotension, particularly when used systematically and in higher doses. Probably this effect is mediated by the release of NO and some prostaglandins.

Of note is the fact that this was not noted with gene therapy.

Hematological side effects in the form of anemia and thrombocytopenia were reported by Lazarous et al. following 5-9 weeks of systemic bFGF administration in dogs. However, these adverse effects have not been reported in short courses of therapy.

The effect of these angiogenic growth factors on neointimal smooth muscle proliferation have not been elucidated yet. Experiments in our laboratory revealed that VEGF enhances re-endothelialization and decrease in neointimal proliferation in a rat carotid injury model (Asahara). Based on this hypothesis our group has treated more than 20 patients following angioplasty, administering the VEGF gene to expedite reendothelialization at the site of balloon inflation. The follows up results of this study are awaited. However, systemic administration of rhVEGF was noted in dogs to exacerbate neointimal accumulations in one study (Lazarous). However, no further evidence has been reported to support this finding either in animal or in clinical studies.

Renal toxicity has also been reported in monkeys receiving 7 days of bFGF (100ug/day). This adverse effect is supposed to be transient and reversible.

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ROLE OF CAROTID DUPLEX SCAN IN DIAGNOSING CAROTID ARTERY STENOSIS

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INTRODUCTION:

The development of carotid duplex scan has revolutionized the diagnosis of carotid artery stenosis. It is now regarded as the most cost-effective and non-invasive screening test for carotid artery stenosis. Carotid duplex scan is highly sensitive and specific for atherosclerotic plaque characterization, determining flow disturbances in extracranial carotid arteries and in grading the degree and progression of carotid artery stenosis. In addition, it also locates aneurysms, dissections, intimal flaps and carotid body tumors. In view of the revised clinical indications for carotid endarterectomy following various multicenter trials, carotid scan has assumed an even greater role in the evaluation of carotid stenosis. However, its accuracy is determined to some extent by the experience and skill of the radiologist.

Carotid duplex scan is one of the diagnostic work up tool for transient ischemic attacks, strokes and for symptoms of vertebro-basilar insufficiency. This scan combines the use of B-mode and Doppler ultrasound to determine the degree of stenosis. B-mode imaging allows a real time picture of intraluminal plaques and surrounding tissues where as doppler ultrasound can assess blood flow using pulsed waves at any point in the field chosen.A high pitched sound audible on doppler suggest high velocity blood flow[1]. A waveform is also seen on the monitor which depicts spectrum of velocities throughout the cardiac cycle. This waveform is recorded at the mid-common carotid artery (CCA), proximal external carotid artery (ECA), proximal and distal internal carotid artery (ICA), and vertebral artery[1].Peak systolic and end-diastolic velocities measured during the various phases of the cardiac cycle are used for grading the severity of carotid stenosis. Recently doppler imaging with color flow, called as color flow duplex (CDI) has proved to be the most accurate non invasive method available[2].The areas of blood flow appear as red or blue depending whether direction of blood flow is towards or away from the transducer beam.Similarly areas of high velocity and turbulence flow are displayed in a mosaic of colors. To ensure accurate velocity measurements and grading of stenosis it is important that correct doppler beam to artery axis is maintained for each segment sampled by the scan.

Various duplex derived velocity and spectral criteria are used for grading the degree of carotid stenosis. All are based on the principle that velocity increases in a stenosis to maintain flow. Less than 50% stenosis causes some turbulence in the blood flow but does increase in velocity significantly. When the lumen diameter is reduced from 50% to 60% systolic velocities increase within the stenosis and pressure drop occurs distally. From 70% to 80% stenosis diastolic velocity also increases. When the diameter is reduced to 95% blood flow velocity decreases to zero[3].The velocity criteria developed by the investigators at the University of Washington is widely used to grade the carotid artery stenosis as normal, 1% to 15%, 16% to 49%, 50% to 79%, 80% to 99% and occluded[4,5]. These categories of stenosis were not used in various retrospective trials of North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST) and hence are no longer applied.

The modification of the University of Washington doppler velocity criteria is used in most centers in categorizing the degree of stenosis and is given in table I below:-

Degree of stenosis	Peak systolic velocity (cm/s)	Peak end diastolic velocity (cm/s)	Remarks
0% to 19%	<125	—	Minimal spectral broadening.
20% to 49%	<125	—	Spectral broadening present.
50% to 79%	<125	<140	Marked spectral broadening present.
80% to 99%	>125	>140	Marked spectral broadening present
Occlusion	No flow.	No flow.	Thump sign in internal carotid artery. Increased flow in external carotid artery and contralateral carotid artery.

TABLE - 1

It is important that each vascular laboratory compares the results of carotid duplex scan with that of a gold standard technique, usually angiography. The

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standardization of duplex and angiographic criteria will help to achieve a more consistent approach in the evaluation of carotid stenosis. Angiography however carries a complication rate of 0.2% to 4%[2]. In symptomatic patients the risk is 7.7% in those with stroke-in-evolution and 12.5% in those with bilateral severe stenosis[2].The risk of stroke alone was 0.7% and 1.2% respectively in NASCET and ACAS trials. Like wise the ACAS (Asymptomatic Carotid Atherosclerosis Study) revealed a lower five year stroke risk when non-invasive tests were used pre-operatively in diagnosing the degree of carotid artery stenosis[6].Angiography also costs ten times more than duplex study. Other drawback of angiography is that the method of measuring carotid stenosis was done differently by various trials resulting in discrepancy in the results. The degree of stenosis was calculated by comparing the residual lumen in the carotid bulb at the point of maximal stenosis to a reference point which was the imagined normal width of the carotid bulb in the ECST study and the distal uninvolved internal carotid artery diameter in the NASCET study. The result was that NASCET underestimated the size of the stenosis in the carotid bulb because the distal internal carotid artery is normally smaller than carotid bulb[2].Similarly ECST could not estimate the true carotid bulb unless it was calcified. The differences between NASCET and ECST methods of measurements became greater for lesser degrees of stenosis. Nicolaides etal reported that 70%, 77%, and 83% ECST stenosis were approximately equivalent to 47%, 60% and 70% respectively of the NASCET stenosis[7].These short comings set limitation in using angiography as diagnostic tool for carotid artery stenosis. Nevertheless angiography is required when duplex is suboptimal or equivocal, in the presence of atypical symptoms or other vascular and anatomical anomalies such as kinking or calcified plaques. Further more duplex scan is unable to assess directly the arch, proximal brachiocephalic and intracranial circulation. Various studies have validated duplex scan against angiography with sensitivity generally about 97% and specificity about 91% in stenosis of greater than 50%[1].The University of Chicago Vascular Laboratory in 1996 found that the over accuracy of carotid duplex scan in stenosis of more than 50% was 95%; in stenosis of more than 80% was 88% and in total occlusion the accuracy was 100%1.The duplex scan however tends to underestimate lower grade stenosis (30% to 49%) and is not useful in such cases[8].Nevertheless atherosclerotic plaque characterization which assumes a greater importance in carotid duplex imaging is now considered an important determinant of stroke. Heterogenous plaque is implicated in embolic disease and acute thrombosis. Patients with intra plaque hemorrhage and ulceration are more likely to be symptomatic. Magnetic Resonance Angiogram (MRA) which is another non-invasive method of analyzing the carotid disease is less reliable than duplex for categorizing stenosis in areas of moderate to severe narrowing[9,10].MRA is an adjunct to duplex or angiography and its definitive role is yet to be determined. In summary it can be safely assumed that carotid duplex scan is a simple, non-invasive technique wherein the degree of stenosis, velocity and character of blood flow and plaque morphology can be accurately measured. It is cost-effective and safe when compared to angiography. Further it is a superior modality in patients with symptomatic high grade stenosis.

However it is highly operator dependent and regular quality assurance is needed to document the accuracy of duplex scan against angiography. Clinical evaluation along with duplex imaging can be used as a main diagnostic method for assessing carotid stenosis prior to surgery with angiography being done only for few selected cases.

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HOARSENESS OF VOICE - AN AETIOLOGICAL STUDY

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***Abstract:**Hoarseness is defined as rough, grating and harsh, vocal disability that may be caused by a variety of causes ranging from a purely functional to serious and life threatening one. Out of 400 patients studied in the present study, 49.75% were having a benign lesion of the larynx, followed by inflammatory lesions 29.2%. Neoplastic lesions were responsible for hoarseness in 4.25% of patients. Though benign lesions are common causes of hoarseness, a detailed evaluation is necessary to rule out malignancy.*

***Key Words:** Hoarseness, Aetiology, Larynx, Symptoms.*

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Introduction

Communication through speach and language is the highest evolved human function for which voice produced by larynx provides the basic wave which is altered by various resonators in the supraglottis, pharynx and oral cavity. Besides being a contributing feature to articulated speech, the voice adds an element of intonation to spoken language which varies in different languages and dialects. In addition the human voice serves a number of non-language communicative functions which are understood by all mankind across language barriers. Thus the voice per se can be regarded as a medium adapted to convey emotional content in the form of articulated speach as is a cultural medium to communicate intellectual content.

Voice production system can be broadly divided into a voice generator (the larynx with its vocal folds) and co-ordinating and controlling function (central and peripheral nervous system). Both these divisions can be affected by functional or organic disease processes. Thus, hoarseness of voice, roughness or harashness of voice can result from a variety of causes ranging from a purely functional or psychological disturbance to a more serious and life threatening condition.

Material and Methods

The present study was conducted on 400 patients of hoarseness of voice who presented to services of otolaryngology of Government Medical College, Srinagar, Kashmir, during a period of one and half year. Detailed history and examination was recorded on a special proforma, particular emphasis was laid on histroy of onset, duration of hoarseness, treatments received. History of occupational and non-occupational voice abuse was particularly asked for. A detailed routine ENT examination focussing specifically on laryngeal anatomy and function was carried out. Wherever indirect laryngoscopy was not possible due to an anatomical abnormality or no-cooperation of the patient, fibreoptic laryngoscopy was carried out under local anaesthesia. Surgical procedures were performed wherever indicated. Rest of the patients were managed by conservative treatment. Final diagnosis as to the cause of hoarseness of voice was made on either response to medical management or histopathology of biopsied/excised specimen.

Observations

400 patients who complained of hoarseness of voice were selected for the study. The age of patients ranged from 4-70 years with mean of 40 years. About 75% patients were males and 25% were females. About half of the patients (45%) were involved in an occupation demanding excessive use of the voice like teachers, preachers, hawkers, certain artisans (Table - I).

Table No.1: Occupation of patients.

S.No.	Occupations	No. of Patients	Percentage
1.	Farmers	100	25
2.	Teachers & Preachers	100	25
3.	Housewives	70	17.5
4.	Shopkeepers	50	12.5
5.	Artisans	30	7.5
6.	Students	30	7.5
7.	Others	20	5

Table No.2: Duration of Hoarseness of Voice.

S.No.	Duration of hoarseness (in months)	No. of Patients	Percentage
1.	0 - 6	180	45
2.	6 - 12	68	17
3.	13 - 24	42	10.5
4.	25 - 36	50	12.5
5.	37 - 36	32	8
6.	49 - 60	28	7
	0 - 60	400	100

Though a good number of patients presented early.

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majority of patients were symptomatic for more than six months before they sought an advice about a change in their voices. The duration of hoarseness of voice prior to presentation is depicted in Table-III.

History of vocal abuse in the form of excessive talking, shouting, screaming, yelling, was present in 250 (62.5%) patients while, 210 (52.5%) patients were addicted to either smoking or snuff. The actual cause for hoarseness of voice in the majority (49.75%) was found to be a benign non-neoplastic lesion of the larynx or an inflammatory lesion. Hoarseness of voice as a symptom for malignant disease was present in 4.25% (Table III).

Benign non-neo-plastic lesions included vocal cord nodules (70.3%) and vocal cord polyps (29.7%). All these cases were treated by microlaryngeal surgery. The study of 117 cases of hoarseness of voice due to inflammatory lesions revealed that most commonly involved age group was between 21-30 years (55 patients) while acute inflammation is a common cause in younger age group (21 patients, 17.94%), chronic laryngitis as a causative factor assumed a significant proporation after second decade (43 patients 36.7%)

Table No.3:

S.No.	Pathologic conditions	No. of Patients	Percentage
1.	Benign lesions (non - neoplastic)	199	49.75
2.	Inflammatory	177	29.2
3.	Paralytic	38	9.2
4.	Neoplastic	17	4.25
5.	Traumatic	9	2.2
6.	Others	20	5
	Total	400	100

Vocal cord paralysis due to various reasons was responsible for hoarseness of voice in 38 (9.5%) patients. Most (17, 14.6%) of these cases were in their fifth decade of life, with an overall male predominance (71.05%).

9(2.2%) patients of traumatic lesions of the larynx leading to hoarseness of voice gave history of blunt external laryngotracheal trauma. No case of penetrating or inhalational or intubation injury was noted in the present series.

Hoarseness of voice was due to bengin neoplastic lesions (vocal cord papillomas) in 5 (29.4%) and due to malignant tumours of larynx in 12 cases-7 had carcinoma of hypopharynx with vocal cord fixation, while 5 had primary vocal cord carcinoma.

Other causes which were found responsible for hoarseness of voice in the present study included dysphonia (14 cases), myxoedema (12 cases) functional (2 cases) and foreign body (paddy grain).

Discussion

Hoarseness is a form of vocal disability where the voice is rough, grating, harsh, more or less discordant and lower in pitch than normal for the individual. This change of voice results from various derangements of laryngeal structure and function. Hoarseness of voice is therefore a symptom and not a disease, the cause for which may lie in the larynx itself or somewhere else where derangement of optimal laryngeal function is the only or one of the several symptomatic expressions. Further it is important that this symptom of laryngeal involvement be taken into consideration seriously and urgently to emphasize the importance of prompt intervention because it may be an early symptom of a serious disease.

The most frequent type of hoarseness seen both in adults and children is that produced by acute laryngitis following a cold or excessive use of the voice[1]. The maximum number of patients with hoarseness of voice seen in the present study were in the age group 21-40 years.

Half of the patients (49.75%) who presented with hoarseness of voice were having benign lesions of the larynx in the form of vocal nodules and polyps. This was followed by inflammmatory lesions of the larynx (29.2%) paralytic lesions (9.5%), neoplastic lesions (4.25%) traumatic lesions (22%) and hoarseness of voice due to miscellaneous causes constituted 5 per cent. All the patients presented with hoarseness of voice irrespective of their age group, sex difference, location and nature of growth. Hoarseness of voice as the chief and or early symptom of benign tumours[2], malignant tumours[1,3,4], paralytic lesions[5] and inflammatory disorders[6] has been widely acknowledged. It is therefore, evident that any hoarseness of voice which doesn't resolve in about a month time (maximum time allowed for an acute inflammatory disorder of the larynx to subside) indicates an immediate and thorough investigation and appropriate treatment not only to improve the quality of life and professional ability in cases of benign lesions but also as a life saving measure in cases of more serious malignant disorders.

Benign (non-neoplastic) lesions: Vocal cord nodules and polyps, are considered as most frequent benign laryngeal lesions[2,7]. The distinction between a vocal polyp and a nodule is considered as a matter of opinion, since histologically both produce identical changes[8].

It is now generally understood that these pathological new growths are the mechanical result of faulty or excessive vocal use. In addition, a vociferous and agressive personality, allergic tendencies and smoking act as predisposing and precipitating factors[9]. These lesions are best treated by microlaryngeal surgery without any consequence. 189 such cases in the present study were treated by direct laryngoscopy and excision under general anaesthesia and the diagnosis subsequently confirmed by histopathology.

Inflammatory Disorders

The second most common (29.2%) group of patients who presented with hoarseness of voice were suffering from inflammatory lesions of the larynx. Th number of acute inflammatory disorders is less (38 cases), probably because our centre acts a referal centre for the whole valley and since most cases of acute inflammation resolve within a week time, they are treated at peripheral health units. Among the 79 cases of chronic laryngitis 30 cases of atrophic type were observed particularly during winter months. Dry hot and smoky environment in a socio-economically low standard population appears to be the reason for this. A significant finding was the presence of 10 cases of laryngeal tuberculosis, all of which were secondary to pulmonary tuberculosis. This finding underlines the importance of investigating chronic hoarseness of voice in cases of pulmonary tuberculosis. Thorough evaluation of chronic hoarseness of voice was rewarding in another case labelled as "chronic laryngitis" but where laryngeal biopsy proved it to be a case of laryngeal carcinoma.

Vocal Cord Paralysis

In the present series 9.5 percent of patients were diagnosed as having vocal cord paralysis. All such cases had unilateral vocal cord paralysis. This finding of hoarseness of voice being primary complaint of vocal cord paralysis is also reported by other workers[10] . However, in the present series the cause for vocal cord paralysis could be found in 13 cases only which included carcinoma oesophagus (6 cases), bronchogenic carcinoma (2 cases), left heart enlargement (2 cases). Rest of 25 were labelled as idiopathic since no cause could be found after thorough investigation. A possible viral aetiology has been proposed in such cases[11]

Neoplastic Lesion

Benign or malignant neoplastic lesion of larynx arising within the larynx or involving it secondarily present primarily with a complaint of hoarseness of voice [10,12,13]. Hoarseness is the presenting symptom in cancer arising from "vocal cord areas" of the larynx (vocal cords, subglottis, intrinsic larynx) which constitutes about 70 per cent of the laryngeal malignancies[14] . Out of 12 cases of malignant tumours involving the larynx in the present series only five cases were that of vocal cord cancer while 7 cases were primarily arising from hypopharynx and involved the larynx only secondarily. In such later cases, hoarseness of voice is a late feature.

Traumatic Lesions

Laryngotracheal trauma either in the form of direct external injury or laryngeal intubation can produce laryngeal haematoma, vocal cord injury or vocal cord granuloma and thereby lead to altered voice. All the 9 cases of laryngeal injury seen in present series gave history of external laryngeal injury and all the patients were managed conservatively.

Summary and Conclusion

A clinical study of 400 cases of hoarseness of voice is presented with the aim of a studying the spectrum of cause responsible for this most common symptom of laryngeal disease. Benign non-neoplastic lesions in the form of vocal cord nodules and polyps are the commonest causes of hoarseness of voice in the hospital attending population in this part of the country.

Acute or chronic inflammation of the larynx is next most common cause for hoarseness of voice, whicle acute inflammation usually accompanies an upper respiratory infection, a high suspicion of tuberculosis or malignancy larynx should be maintained in more chronic forms of non-resolving hoarseness of voice.

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ENDO UROLOGICAL DIAGNOSIS AND TREATMENT OF HAEMATURIA

R. Nagar M.S.; Satish Sharma M.S.; Sunil Gupta M.Ch.; C.L. Gupta MS.

Abstract: *This study has been carried out on 108 patients of haematuria, 66% patients were males and 24% patients were females. Mean age of the patients in the study group was 50.12 years. All the patients were subjected to a battery of investigations ranging from routine urine examination to urinary cytology, trans abdominal ultrasonography, intravenous urography, CT scan, cytopanedoscopy and ureteroscopy. After having established the diagnosis, the patients were subjected to endourological treatment and open surgery. It was seen that the endo-urological evaluation of the disease and the treatment had an advantage over the other methods of diagnosis and treatment.*

Keywords: *Bladder, haematuria, Lithotripsy, Uretero renoscopy.*

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Introduction

Haematuria[1] is one of the most important symptoms of urinary tract diseases. Sight of blood in urine is alarming for the patient and challenging to the clinician, as it poses a great problem in locating site and identifying the cause of bleeding. Normally 1-2 million of RBCs per high power field are seen in a centrifused sample of urine. When quantity of RBCs increases beyond the normal range, haematuria is said to be present. Aetiology of haematuria has been variable ranging from a number of systemic causes, renal causes, causes in urinary tract including causes with no pathological basis for any explanation.

Endourology[3] is a rapidly growing field and many of its innovative techniques and instruments are practicable for an average urologist to diagnose and treat various urological diseases which are causes of haematuria without open surgical procedures.

Material and Methods

This study has been conducted on 108 patients admitted in the Department of Surgery, Govt. Medical College, Jammu for a period of one year. All the patients were subjected to routine investigations like haematological, kidney function tests, urinary cytology, KUB and Intravenous urography and transabdominal ultrasonography and CT scan. Besides these endo urological procedures like cystopanendoscopy, ureterorenoscopy, transurethral resection biopsy and urinary bladder washing irrigations were carried out in these patients. In majority the endourological management was contemplated while in others open surgical procedures were done. The results of the endourological diagnosis in form of efficacy method adopted, operative time, post operative complication, hospital stay and time to return to work.

Observations

Study group included the age ranging from 4 years to 90 years. Mean age was 50.12 years. Male to female ratio was 3.1:1.

Duration of haematuria — from one day to more than 2 years.

Distribution of Aetiologies

Majority of the cases, 37.04% had carcinoma of urinary bladder[12], 19.44% had benign prostatic hyperplasia 3.70% had carcinoma of prostate. Besides these other causes were vesical calculus, renal calculus, posterior urethritis, cystitis, tubercular cystitis, post irradiation cystitis, renal pelvic-ureteric tumor, renal cell carcinoma[4] and wilm's tumor.

Diagnostic Accuracy

Ultrasound[2] is more helpful in carcinoma of urinary bladder, prostatic diseases and in renal tumors. Intravenous urography is very useful in detecting renal tumors[5], urolithiasis and carcinoma of urinary bladder. It could identify 65% lesions of urinary bladder. CT scan is conclusive in most of the urinary tract tumors and also showed the lymph node status. Cystourethroscopy is an excellent approach in detecting the cause of haematuria in lower urinary tract, success rate was 100%.

Uretero Renoscopy[3,6] was done in 8 cases only. It could locate the exact site of ureteric calculi lower ureteric tumor

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was seen in one of the cases.

Endoscopic surgical procedures were undertaken in 72 cases. 36 cases were subjected to open surgery and conservative management in toto.

Complications

Post operative haematuria was seen in majority of endoscopic procedures. Besides stricture urethra developed in 14% patients who underwent TUR of prostate. Two patients suffered from ureteral injury[7, 9] following uretero renoscopy and required DJ stenting.

Stay in the Hospital

72% of the patients after various endoscopic procedures were discharged on fourth post operative day. 15% of the remaining patients were discharged within eight days. In open procedures majority of the patients stayed for more than eight post operative days. One patient after total cystectomy remained in the hospital for more than forty five days.

Discussion

This study was carried out while still introducing the technique of uretero renoscopy diagnostic as well as treatment of upper tract ailments. Therefore learning curve was present during the phase of study. Nevertheless we learned from our failures and tried to improve upon our technique.

Mean age of the patient was 50.12 years with a range from 4 to 90 years. More than 71% of patients were above the age of 40 years.

MC Carthey et al 1980 have confirmed that 97% of cases with carcinoma urinary bladder and other malignancies were above the age of 40 years. Aetiology of haematuria varies from conditions posing minimal risk to the patients such as cystitis, urethritis, to potentially life threatening conditions like urinary malignancy, same has been observed by workers like Abuelo 1983. Diagnostic accuracy of ultrasound ranged from 66% to 100%. Intravenous urography detected the lesions in over 52% cases. Intravenous urography offers advantage over other investigative procedures that it can tell about the status of renal functions. CT scan is an accurate measure in the evaluation of renal masses and provides extra organ involvement evidence.

Cystopanendoscopy offers the advantage over the other modalities in accuracy and has distinct advantage over radiography and ultrasound in that the lesions can be seen and biopsied. In addition to accurately diagnosing the disease, other characteristics seen only with cytoscope are exact size, shape, character, position and involvement of ureteric orifices. Besides urinary bladder tumors and prostatic diseases can be identified and treated with transurethral resection.

Uretero Renoscopy could diagnose the site of calculi in one case. We could detect the lower ureteric tumor. similar observation has been made by Booth et al (1980). However, upper ureter could not be visualised. Transurethral resection[10] was done in urinary bladder tumors and then depending upon the histopathological examination further treatment was carried out after having established the stage and grade of the disease i.e. post operative radiotherapy, chemotherapy and cystectomy.

Vesical lithotripsy was done in 84% cases of vesical calculi with ultrasonic lithotripsy.

Ureteroscopic removal of calculi[11] from lower ureter was tried in all the patients with success in only 75% of the patients. Though it does not match with the success rate of extraction of stones by various workers from 90% to 98% (Hyon et al 1984) we were satisfied by our success as we are still in learning curve stage.

In the remaining cases open surgical procedures were adopted. A few post operative complications were seen. One case was reported with post operative stricture urethra in the follow up period. Urinary tract infection was seen in 10%-15% cases whereas in open surgical procedures infection rate was 35%, upper urinary tract infection was seen in the case in whom total cystectomy was done thereby increasing the post operative stay in hospital for more than 45 days.

In ureterorenoscopy, ureteral injury was noticed in 165 cases. The rate of ureteral injury in various centres reported is 11%-17%. Mild haematuria aetiologies are treated with endoscopic urological procedures. These have led to a very little scope for open surgical procedures.

Besides the average convalescent period after endoscopic procedure was 4.7 days including the stay encountered with major endoscopic complications, where as it was 11.7 days on an average in open surgical procedures. The morbidity with endoscopic procedures is less and better patient tolerance and resumption to work is earlier as compared to open surgical procedures.

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"ROLE OF INTERMITTENT CLOBAZAM IN FEBRILE SEIZURES"

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Abstract: 45 Children, 25 female and 20male with ages ranging from 3 months to 7 years that experienced at least one febrile seizure were taken up for a prospective study, of intermittent treatment with clobazam. Patients with afebrile seizures, seizures during CNS infection and neurological abnormalities were excluded. Parents of 5 children could not be contacted. So only 40 children were taken for the study. Seizures were of different types i.e.grand mal in 25, complex partial in 10 and unclassified in 5. Patients were followed up for 1 year. Clobazam was given orally during the febrile episode according to body weight, 5mg/day upto 5Kg, from 5Kg to 10Kg 10mg/day, from 11Kg to 15 Kg 15mg and above 15Kg 20mg/day. There were 100 febrile episodes with temperature above 100°F. Drug efficiency was assessed by recording recurrence in the febrile episodes that were treated with Clobazam + antipyretic with those in which only antipyretic drugs were given. Of the 60 febrile episodes treated with clobazam and antipyretic there were only 2 recurrences (3.33%) while of the 40 febrile episodes treated only with antipyretic measures there were 10 (25%) recurrences. Adverse effects occurred in only few patients (5) and consisted of vomitting and somnolence, and these symptoms occurred only in some episodes and were absent in other episodes. We conclude that clobazam is safe and effective in preventing FS recurrences, it may be an alternative to diazepam in the intermittent treatment of FS recurrence.

Key words: Febrile, Clobazam, Seizures

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Introduction

One of the most common neurological disturbances in children are febrile seizures with an estimated incidence of 2-5%.[1-7] Children that have experienced FS have a slightly higher incidence of epilepsy than the general population[1]. The recurrence rate of FS in a child varies from 25 to 50%, depending on the age at onset, 50% have their second episode within a 6 month period after the first episode, 75% within one year and 90% within 2 year[7-8]

Treatment of FS is a controversial issue, in face of its benign course and of the adverse effects of antiepieptic drug administration especially in infancy. Various therapeutic approaches were tried. Continuous treatment with phenobarbitone and later with sodium valproate were used for many years, but are now abandoned due to the incidence of adverse effects and to lack of efficacy. Several studies reported efficacy of intermittent diazepam in febrile episodes in prevention of FS recurrence[4,9,10,11,12].

Methodology

Children were selected between 3 months and 7 years of age, they had experienced one or more FS. Children with a febrile seizure during CNS infection and neurological abnormalities were excluded. During the initial visit a detailed medical history was taken. A detailed neurological examination was performed and parents or literate members of the family received a diary and were instructed to note down the medicine used and seizure recurrence. They received information concerning antipyretic drug and clobazam usage according to childs age and weight. They were instructed to administer clobazam orally during febrile episodes according to the schedule shown in table I.

Results

Forty children were taken up for the study, family history of epilepsy was present in 8 cases and of febrile seizures in 10. Grand mal seizures occurred in 25, complex partial in 10 and unclassified in 5. Patients were followed up for one year. Clobazam was given orally during the febrile episode as shown in table I. By comparing FS recurrence in the febrile episodes that were treated with clobazam plus antipyretic with those in which only antipyretic drugs were given drug efficacy was measured. Of the 60 febrile episodes treated with clobazam and antipyretic there were only 2 recurrences (3.33%) while of the 40 febrile episodes treated only with antipyretic measures there were 10 (25%) recurrences. Adverse affects occurred in only 5 patients and consisted of

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vomiting and somnolence and occurred only in some episodes.

TABLE I

Clobazam dosages according to weight

Weight	Dosage
Upto 5Kg	5mg/day
6-10 Kg	5mg B.D.
11-15Kg	7.5mg. B.D
> 15Kg	10mg. B.D.

Discussion

For febrile seizure recurrence prophylactic treatment has been criticized by many authors as they have benign outcome and antiepileptic drugs have various adverse effects[6,13,14,15,26]. Phenobarbitone causes cognitive impairment and hyperkinetic behaviour on long term use[16,7]. Another drug used for prophylaxis i.e. valproic acid causes severe adverse effects especially in infants[3,16]. The decision of not treating FS implies in the risk of seizure recurrence during febrile episodes. There are reports of relationship between temporal lobe epilepsy and prolonged febrile seizures in infancy[18-22]. These studies brought back the issue of FS treatment preferably with drugs that are effective and have few adverse effects. Benzodiazepines, given only during the febrile episodes, were found to be effective in FS recurrence in several studies with few adverse effects[4,9,10,11,12]. In the present study the results showed that in 60 treated febrile episodes there were only 2(3.33%) recurrences while among the 40 untreated episodes there were 10(25%) recurrences. Manreza et al[24] reported a recurrence rate of 1.75% in a group treated with intermittent clobazam in comparison to 22.99% recurrence rate in untreated group. Londi et al[24] reported a recurrence rate of 2.6% in a group of 39 children treated with intermittent clobazem. These recurrence rates are lower than those observed in studies that used intermittent diazepam where 5 to 29% recurrence rates were found[11]. Adverse effects were found in only 5 patients in our study and were mild and were not consistent. We conclude that clobazam is safe and effective in preventing recurrence of febrile seizures.

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CLINICAL PROFILE OF SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE) IN KASHMIR VALLEY

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Abstract: *Subacute sclerosing pan encephalitis (SSPE) is a rare disese, with fewer than 10 cases per year reported in United States. The incidence has declined substantially since the introduction of measles vaccine. We conducted a retrospective study of 25 patients diagnosed from Jan. 1994 to Dec. 1998 in SKIMS. Most of the patients belonged to low socioeconomic stauts; with a definitive history of measles in 21 (84%) of patients. 18(72%) patients were more than 8 years of age at the time of onset of symptoms. More than 50% patients (13) presented in stage II of the disease Oligoclonal bands in CSF was positive in 20 patients (80%).*

Keywords : *Subacute seterosing Penencephalitis, neasles, digoclonal bands.*

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Subacute sclerosing pan encephalitis (SSPE) is a progressive slowly evolving viral disease affecting children and young adults(1). It is characterized by periodic myoclonic jerks with progressive fatal encephalopathy, typical electroencephalographic (EEG) changes, increased oligoclonal IgG and high measles virus antibody titres in serum and cerebrospinal fluid. Its pathogenesis has not been fully clarified, although isolation of causative agent that is antigenically similar but not identical to measles virus has been accomplished in a large number of cases.

In west immunization against measles has greatly reduced the incidence of SSPE(2) but in India it still remains a significant cause of morbidity and mortality(3). The data from India is limited about SSPE(3,4). No population based data on SSPE is available from India. However, hospital based studies from Bombay(3), Pune(5), Delhi(6), Chandigarh(7) and Bangalore(8,9) reported a high frequency of SSPE compared to west. Lack of awareness about immunization against measles, and overcrowding, particularly among lower socioeconomic group probably accounts for increased incidence of SSPE in India. We undertook a retrospective analysis of patients with SSPE seen at Sher-i-Kashmir Institute of Medical Sciences to study the clinical profile of the disease and look for common manifestations of disease in Kashmiri population.

MATERIAL AND METHODS

Sher-i-Kashmir Institute of Medical Sciences is a tertiary referral centre for neurological diseases and receives patients from all over Kashmir valley, Ladkah region and parts of Jammu region. The medical records of 25 patients with subacute sclerosing panencephalitis diagnosed in the Deptt. of Neurology during the period from January 1994 to December 1998 were reviewed in detail. SSPE was diagnosed if the patient fulfilled any three of the following five criteria modified from Dyken(10).

1. Typical clinical presentation.
2. Typical EEG pattern with stereotyped periodic complexes.
3. Typical histological findings on brain biopsy or autopsy.
4. Elevated cerebrospinal fluid(CSF) globulin levels greater than 20% of total CSF protein.
5. Elevated CSF measles antibody titre of 1:4 or more by haemagglutination inhibition or 1:20 or more by enzym-linked immunosorbent assay (ELISA).

Staging of SSPE was done according to modified Jabbour criteria(11) as follows:

Stage I - Mental and behavioral changes, forgetfulness, irritability and lethargy.
Stage II - Myoclonic jerks, dyskinesia, choreoathetosis, ataxia.
Stage III- Decrebrate rigidity and decorticate rigidity

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Stage IV - Loss of cortical function, flexion posturing of limbs and mutism No brain biopsy or autopsy was done in our cases

RESULTS

25 patients of SSPE included 18 males and 7 females with age from 3 - 19 years. Most of the patients belonged to low socioeconomic status. A definitive history of measles was available in 21(84%) of patients of whom 17(68%) had measles after 3 years of age. 18(72%) patients were more than 8 years of age at the time of onset of symptoms.

Table I: Age at onset of symptoms

	No. of cases	%age
0 - 4	2	8
4 - 8	5	20
8 - 12	15	60
> 12	3	12

Table II: Duration of symptoms prior to presentation

	No. of cases	%age
0 - 6	4	16
7 - 12 months	5	20
13 - 24 months	13	52
> 24 months	3	12

The initial interval between measles infection and onset of symptoms of SSPE ranged from 26 months to 12 years. Six patients had an interval of more than 8 years between the initial attack of measles and subsequent development of SSPE. Majority of patients had symptoms for more than 12 months at the time of presentation.

3 patients presented in stage I, 13 patients presented in stage II, 7 patients in stage III and 2 patients in stage IV disease. Age at onset and duration of symptoms prior to presentation in the hospital are shown in Table 1 and 2 respectively while table 3 shows the stage of disease at the time of presentation. The details of dominant clinical features at the time of examination are shown in table IV.

CSF examination was performed in all the 25 cases. Three of the CSF samples revealed pleocytosis but protein was elevated in 18 cases(72%) with a range of 60 - 140 mg%. Oligoclonal bands were +ve in 20 out of 25 cases (80%). Antimeasles antibody titres were significantly elevated in CSF and in serum in 21 cases.

EEG examination was carried out in all cases and repeated wherever indicated. The EEG findings are summarized in table V. Periodic complexes were seen in majority of patients studied at the time of presentation irrespective of the stage of disease. In three patients EEG had to be repeated after an interval as the initial EEG was inconclusive. The patients in stage IV had burst suppression along with periodic complexes. All the patients who presented in stage II had normal background and periodic complexes whereas in all the patients in stage III background showed a gross slowing. Computed tomography(CT) scan was performed in all the patients and only in five cases did it show abnormality consisting of generalized brain edema in 3 and significant cortical atrophy in 2 cases.

Table III: Stage of disease at presentation

Stage	No of cases	%age
I	3	12
II	13	52
III	7	28
IV	2	8

Table IV: Clinical features of SSPE (n-25)

	No.	%age
Decreased scholastic performance	23	92
Myoclonus	17	68
Extrapyramidal rigidity	15	60
Pyramidal signs	12	48
Speech disturbance	10	40
Sphincter disturbances	11	44
Gen. tonic clonic seizures	8	32
Visual disturbances	3	12
Cerebellar signs	7	28

DISCUSSION

Subacute sclerosing panencephalitis is a slowly progressive degenerative disease of the central nervous system(CNS) in childhood and adolescence secondary to aberrant viral genome expression and non-productive persistent viral infection of neural cells by defective measles virus not expressing its M protein. In terms of morbidity and mortality SSPE is the commonest persistent viral infection in children in India and primary reason for this is the high prevalence of measles. The relationship between measles and SSPE is firmly established (9,12,13) and measles virus has been isolated from cultured brain cells of patients with this disease(14).However, history of measles is obtained in only 25-51% of patients with SSPE in India(5,6). 10 patients in the present study had no antecedent history of measles but still developed the disease. A subclinical infection probably accounts for such phenomena(2).

The classical stereotyped clinical course of patients with SSPE has been described in 4 stages by Jabbour et al in 1969. Only three patients in our series presented in stage I. All others presented in stage II onwards. This could be because of earliest symptoms of behaviour changes and poor scholastic performance being unnoticed in children in the absence of other symptoms and signs. Rapid progression is well known feature of the disease(1). However, in our study, 16 patients had symptoms for more than one year before presentation which could be explained in terms of phasic illness affecting different sites as also proposed by Cobb(15). This delayed progression of disease could be because of containment of infection due to vaccination(16).

Table V: EEG findings in SSPE (n = 25)

Background	No.	%age
Normal	15	60
Slow	10	40
Periodic complexes	22	88
Rhythmic delta waves	2	8
Paroxysmal sharp waves	1	4
Focal abnormality	4	16

The clinical features in our patients differed little from those reported in the literature(10,11). SSPE is a disease of childhood, the most likely age group affected being 5-15 yrs(17). Our study showed a similar trend. The occurrence of SSPE in boys is about 2-4 times greater than in girls(10,11). Sex difference in our study also correlates with other studies done from various parts of India. Most of our patients presented in stage II. The common presenting features were cognitive decline and myoclonic jerks. Other features were pyramidal and extrapyramidal disturbances, speech difficulties and sphincter involvement and there was no difficulty in diagnosing such patients. However, patients with uncommon presenting symptoms like generalised tonic clonic seizures, visual disturbances and altered sensorium posed difficulty in initial diagnosis.

The ocular manifestations of SSPE include focal choreoretinitis, nystagmus, papilloedema and optic atrophy(18). Fifty percent of patients with SSPE have some ophthalmic manifestations at some stage of the disease process(18). Five patients had ophthalmic manifestations in present study which conforms with reported literature. Cortical blindness, which is a rare phenomena in SSPE, was present in one of our patients with normal cranial CT scan and the diagnosis was established by finding of periodic complexes in the EEG. Waxy macular degeneration and papilloedema was seen in two of our patients in early stages of the illness which is also an unusual finding(18).

The wide variation and distribution of the encephalopathic process and variable rate of disease progression probably accounts for the variable clinical presentations(19,20). EEG changes seen in the present study are consistent with those reported earlier(14). Normal background seen in patients who presented in stage I is well reported(21). No correlates could be drawn between focal abnormalities detected in EEG and cases with associated generalised tonic-clonic seizures. Out of the 25 CT scans performed 20(80%) were normal which is consistent with other reports.

The variable presentation of SSPE cases should always be kept in mind while dealing with unexplained prolonged encephalopathic illness in children and adolescents. Even in cases with uncommon manifestations of SSPE, EEG and CSF examination were enough for arriving at reasonable and correct diagnosis.

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A COMPARATIVE STUDY OF PROSTAGLANDIN E2 GEL (INTRACERVICAL) VERSUS OXYTOCIN DRIP IN INDUCTION OF LABOUR

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Abstract: *Two hundred patients upto the age of 35 years with the gestational period between 37 to 42 weeks formed the material, which were divided into two groups of one hundred patients each. The progress of labour was assessed in PGE2 and oxytocin administered groups. Intracervical administration of PGE2 resulted in remarkable improvement in Bishop Score compared to Oxytocin infusion groups. The difference between the two groups which remained undelivered after 24 hours in this regard was highly significant statistically (t value 5.14). Apgar score of new born babies at one minute was greater in group A and the two groups differed significantly in this regard.*

Key words: *Bishop Score, Prostaglandin E2*

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Introduction

The labour starts spontaneously at term; its induction is required at or near term wherever the mother and the fetus are at risk[1]. There are different techniques for induction of labour. The administration of dilute solutions of oxytocin intravenously was introduced by Theoblad et al 1948[2]. Intravenous infusion of Oxytocin is widely accepted as an effective and safe method for induction of labour. However, the out come of Oxytocin induction is highly dependent on the state of cerix[3]. It is now established that both prostaglandin E2 and F2 alpha can induce labour when administered intravenously[1,4,5]. However since the prostaglandins are to be categorized as locally acting hormones, they should be administered peripherally as close to the organ as possible. Such an application will give optimal efficacy with minimum side effects. Intracervical instillation of PGE2 gel (Dinoprostone gel) is a safe and a more effective method of inducing labour in patients with a poor Bishop Score. The complictions are lower with minimum failure rates.

The present study was conducted to compare the effectiveness of intracervical application of PGE2 gel (Dinoprostone gel) with intravenous infusion of oxytocin for induction of labour.

Material and Methods

The present study was conducted on 200 pregnant patients with gestational age between 37 to 42 weeks for elective induction of labour in obstetric wards of Government Lal Ded Hospital, Srinagar. The patients were divided into two groups. Group A, comprised of 100 patients, where induction was done by intracervical administration of PGE2 gel. Group B comprised of 100 patients, where induction was done by intravenous infusion of Oxytocin. Inclusion criteria of patients was, gestational age between 37 to 42 weeks, age upto 35 years, vertex presentation, good fetal heart, adequate pelvis, intact membranes and patients not in labour. A detailed history, examintion and baseline investigations were carried out on all the patients, including an informed consent. Pervaginal examination was done in each case to asses the pelvis. Bishop Score was determined with a sterile technique.

The progress of labour in patients included was assessed and careful watch was kept on fetal heart rate, maternal pulse, blood pressure and type of uterine contractions. The induction delivery time was calculated in group A from application of intracervical PGE2 gel to the completion of delivery and in group B from the first oxytocin infusion to the completion of delivery. Condition of the new born was assessed by one and five minute Apgar score.

Results:

In Group A the indication of induction of labour was, postdated in 55 patients, pregnancy induced hypertension in 39 patients and bad obstetric history in 6 patients, while as in group B the number of patients with these indications was 57, 35 and 8 respectively.

In Group A 25 patients (25%) 7 had favourable cervical state (Bishop Score >5) while 75 patients (75%) had unfavourable cervical state. (Bishop score<5). In

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Group B, the number of patients was 35 and 65 respectively.

Table-1: Showing Bishop Score in different group at various stages of assessment with final mode of deliver

Group of Patients		A	B
Total No. of Patients		100	100
Number of patients with %age induced with unfavourable cervix.		75(75%)	65(65%)
Preinduction Bishop Score	Man	3.11	3.52
	Range	1-5	3-4
Post Induction Bishop Socre	Mean	6.22	7.05
	Range	6-8	6-8
5 hours after induction Difference in mean		3.11	3.43
Number of patients delivered within 24 hrs.		41	16
%age of patients delivered		56.6%	24.6%
Z-value of probability		Z=4.38	

Table-II: Table showing - Bishop score in different groups at various stages of assessment in undelivered patients.

Group of Patients		A	B
Pre-induction Bishop Score	Mean	2.3	3
	Range	1-4	1-4
Post Induction Biship score 5 hrs. after induction	Mean	5.6	3.08
	Range	5-8	1-4
	Difference	3.3	0.08
t-value 5 hrs. after induction			t value = 6.63
t-value 24 hrs. after induction			t-value=5.14

Table-III: Showing 1 and 5 minutes apgar score of neonates born in two groups.

Group	1 Minute Range	Mean	5 Minutes Range	Mean	1 Minute Standard Error & S. Deviation	5 Minutes SE &SD
A	6-9	7.7	8-10	9.5	SE = ±0.64 SD = 0.63	SE = ±0.53 SD = 0.54
B	6-9	7.72	9-10	9.42	SE = ±0.83 SD = 0.81	SE = ±50 SD = 0.5

1 Minute t value = 2

5 Minutes t value = 0

Discussion

In the present study, Group A comprised of patients with period of gestation between 37-42 weeks with mean gestation age of 40.2 weeks with standard error (SE±1.68) and variants of 1.68. Group B comprised of patients with periods of gestation between 38 and 42 weeks with mean gestational age of 39.9 weeks. The standard error being (SE=+1.41) and varians 1.42. Similar matching of gestational age were made by Ulfulmsten ulmsten et al 1979[6] Gunyor Eleman et al 1982[7], Kenneth F. Trofatter et al 1985[8], Krishna Mukherjee et al 1996[9].

Elias et al 1972[5] studied 14 primigravidae and noted that there was difference in mean induction delivery time of primis (3-7 hours) and multis (8-9 hours). They concluded that mean induction delivery time had some relation to pre-induction Bishop Score. Similar observations have been made by other authors viz Krishna Mukherjee et al 1996[6].

Testing the difference between PGE2 gel and oxytocin infusion in patients with unfavourable cervical ripening who delivered within 24 hours is highly significant as the z value of probability is very high (z=4.38) at 56°F which implies that PGE2 gel a much more efficient drug than Oxytocin used for induction of labour which in turn is dependent on cervical ripening. This was comparable to many studies where Bishop scoring was a clinical part of trial. Ulfulmsten et al[6], Carl Nimrod et al, Krishna Mukherjee et al 1996[9]. Thus rate of caesarian section in PGE2 gel is less than oxytocin infusion Similar results were observed by Ulfmesten et al[6].

Twenty patients having favourable pre-induction Bishop Score when treated with PGE2 gel delivered within 24 hours and no patient remained undelivered. In the oxytocin treated group 20 patients (83.1%) delivered within 24 hours and no change in Bishop score was noticed in 4 undelivered patients. Krishna Mukherjee 1996[9] concluded that 73% cases, were induced by PGE2 gel intracervically and 26.5% were induced by oxytocin alone. The caesarian section rate was higher in oxytocin group (40.0%) as compared to PGE2 induced patients (16.36%). Vaginal delivery was 83.66% in PGE2 group as compared to oxytocin induced patients (60.0%). There was no significant difference in Apgar score vis a vis PGE2 and oxytocin infusion (t value =0). Ulfulmesten et al 1979[6] concluded in his study that all children were delivered in good condition with 5 minutes Apgar score of 7.7.

S. Stamp sorensen et al[10] concluded in his study that in patients delivered in the course of the first two days, the Apgar score in all infants of women in PGE2 induced group was 8 or higher at 1 minute and 10 at 5 minutes.

One patient receiving PGE2 gel and two patients receiving oxytocin infusion required delivery by vacuum extraction because of acute fetal distress in late second state of labour. No complications were observed in the study which is consistent with the work done by Ulfulmsten[6].

Conclusion

There is a positive correlation between the initial Bishop Score and success of induction by pharmacological intervention. Intracervical administration of PGE2 gel in patients with favourable pre induction Bishop Score results in 100% successful induction within 24 hours of its administration. Patients even with unfavourable pre induction Bishop Score (BS<5) are also helped by local administration of PGE2 gel in way of improving Bishop Score more efficiently than oxytocin infusion. Technique of local administration of PGE2 gel is simple, more reliable and has higher patient acceptability. It has no antidiuretic effect which may be an asset if labour is to be induced in patients with PIH and cardiac disease.

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NEONATAL RISK FACTORS AND OUTCOME OF BIRTH ASPHYXIA

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Abstract: *The Present work was undertaken to study birth asphyxia related morbidity and mortality in association with neonatal risk factors. A total of 1615 babies were delivered at the institute of Medical Sciences, Soura during 1992-93, out of whom 69 babies (4.18%) had birth asphyxia. The study group comprised 369 babies, which included all the 69 asphyxiated ones. The control group included desired sample of 200 non-asphyxiated babies. Mothers of both the study and the control groups were also studied for maternal risk factors and associated problems. As mentioned above, 69 babies (4.18% of total deliveries during the study period) had birth asphyxia. The ratio of percentage of male to female asphyxiated babies was observed as 1.7;1. Seven (10%) of the asphyxiated babies were preterm (<37 weeks), and 26(38.5%) had birth weight of less than 2.5 kgs. All except two babies (3%) were born spontaneously. Birth asphyxia was anticipated in 18(26%) of the asphyiated newborns by clinical monitoring and 14(20%) were associated with placental weight of less than 400 gms. Neonatal, orbidity included respiratory distress (n=20), apneic spells (n=15), hypothermia (n=20), hyperbilirubinemia (n=10), septicemia (n=10), convulsions (n=7), feeding difficulty (n=8) and necrotising enterocolities (n=3). Eight (12%) of the asphyxiated babies died, majority within first 24 hours of life. Neonatal Morbidity and mortality was definitely increased with birth asphyxia, especially in severely affected ones. Therefore, careful monitoring of newborns during labour and employment of appropriate measures need to be undertaken to prevent birth asphyxia.*

Key words: *Birth asphyxia, Morbidity, Mortality, Placental weight, Preterm.*

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Introduction

Birth asphyxia is one of the leading, though potentially preventable cause of perinatal morbidity and mortality. About 5-10% of babies experience some difficulty in initiating breathing[1]. Asphyxia neonatorum can be anticipated by recognition of certain high risk maternal factors[2]. But, surprisingly some babies may be born asphyxiated without any evident predisposing cause. Much work has been done regarding the late mental prognosis of babies having asphyxia at birth but immediate complications and outcome of such babies has not been well documented. The present series attempts to find the incidence of birth asphyxia and document the immediate clinical complications with morbidity and mortality profile of asphyxiated reonates in a hospital based study., the first of its kind reported from the Kashmir Valley.

Material and Methods

This study was done in the departments of Neonatology and Obstretics, Institute of Medical Science, Soura, Srinagar, during the year 1992-93. A census based technique was adopted among axphyxiated babies. 369 mothers were included in the study and detailed information was recorded regarding maternal diseases, socio-economic factors, pregnancy and obstretic complications. Every mother whosoever attended the hospital for delivery was monitored from the first stage of labour till its terminal phase. All the cases of birth axphyxia (n=69) were included in the study and simultaneously for the sake of comparison, the desired sample of 200 mothers with non-asphyxiated babies was acquired as per the mentioned sampling technique.

Each and every delivery was attended by paediatric resident and apgar scoring was done at one and five minutes after birth by the method adopted by Virginia Apgar[4]. The events after birth were timed accurately by a stop clock. Neonates with one minute apgar score of less than 8 and/or babies with lack of spontaneous breathing at one minute after birth were included in the study. Accordingly, birth asphyxia was classified as mild, moderately severe and severe grades with total scores of 6-8, 4-6 and 0-4 respectively[4] Endotracheal intubation was done in infants with one minute apgar score of zero

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or deterioration occuring despite adminstration of oxygen with Ambu bag and face mask. Injection Vitamin - K(0.5 mg) was given to all asphxiated babies. Prophylactic antibiotics were started in cases associated with prolonged rupture of membranes and frequent pervaginal examinations before delivery. All the aphyxiated new borns were admitted to neonatal intensive care unit for close monitoring during the first 24-48 hours of life. Thirty seven cases received 5-10ml of 7.5% (1:1 diluted) sodium bicarbonate in doses of 2-3ml/Kg body weight. Neonatal risk factors, morbidity and mortality in asphyxiated babies were recorded accordingly.

Results

Incidence

Out of 1651 infants delivered during the study period, sixty nine (4.18%) had birth asphyxia.

Neonatal Risk Factors:

Birth asphyxia incidence was more in males and the ratio of % of males to females was 1.7:1 (Table-1). Seven (10%) babies were preterm (37 weeks), 58 (84%) were of 37-42 weeks gestation and four (6%) were of beyond 42 weeks. Seventeen (25%) babies were small for date while 26 (38%) were of low birth weight.

Table-I: Association of Neonatal Sex with Birth Asphyxia

Sex of Newborn	Total Newborns No(%)	Birth Asphyxa No(%)	Statistical Inference
Male	87 (24)	24 (28)	$x^2 df_1 = 5.91$
Female	282 (76)	45 (16)	$p < 0.02$ (Sig)
Total	269 (100)		

During the course of delivery of 369 babies, 37 (10%) babies had evidence of acute foetal distress and the incidence of birth asphyxia in such babies was 49%. Forty four (44%) of the asphyxiated babies were delivered spontaneously, 23 (33%) by forceps / vacuum and two (3%) by lower segment caesarean section. While detecting the influence of placental weight on birth asphyxia, it was found that in 14(20%) cases the placental weight was less than 400 grams (Table-II).

Table-II: Association of Placental Weight with Birth Asphyxia

Placental weight (Grams)	Birth Asphyxia NO = 69	Statistical Inference
< 400	14 (20%)	$x^2 df_2 = 22.72$
400 - 500	22 (32%)	$p < 001$
> 500	33(48%)	H. Sig.

Neonatal Morbidity

The neonatal morbidity included respiratory distress (n=20) hypothermia (n=20), apneic spells (n=15), ECG changes (n=12), hyperbilirubinemia (n=10, septicemia (n=10) feeding difficulty (n=8), convulsions (n=7) and necrotising enterocolitis (n=3).

The various clinical entities causing respiratory distress included, meconium aspiration, hyaline membrane disease, transient tachypnoea of new born and pneumonia. Out of the fifteen babies who developed repeated apneic spells, seven were associated with other disorders like respiratory distress syndrome (n=3), seizures (n=2), septicemia (n=1), and intraventricular haemorrhage (n=1). Almost all the infants with isolated apneic attacks were less than 34 weeks of gestation. ECG changes like ST segment depression and T-wave inversion were seen in all leads in 11 babies and one baby had features of LBBB (Wide QRS in V1 and V2 and M-shaped QRS complexes in V2 V# and V4).

Hyperbilirubinemia (total serum billirubin exceeding 12 mgms/dl in term and 14mgm/dl in preterm babies) was found in 20 infants including 10 (14.5%) of the asphyxiated ones. Among asphyxiated babies it was due to Rh and ABO hemolytic disease (n=2), septicemia (n=1) and in 7 cases due to predisposing factors like hypoxic liver injury (which was documented by raised liver enzymes) cephalhaematoma and prematurity.

Seizures developed in seven newborns within first 12 hours of age. These were mostly due to cerebal edema with or without intracranial bleed except in two cases where hypocalcemia and hypoglycemia (one case each) were the underlying problems. Clinical manifestations of necrotising enterocolitis developed in 3 babies after 48 hours of life. All these complications developed in severely asphyxiated babies except 6 moderately asphyxiated cases who developed hypothermia.

In the control group, 15 babies developed hyperbilirubinemia (total serum bilirubin >12 mgs/dl). In 11 (5.5%), the same was explained on the basis of physiological jaundice of newborn and in the remaining 4(2%) it was due to Rh and ABO hemolytic disease. Further, 7 babies (3.5%) developed hypothermia because of unnecessary transportation to neonatal ward in cold weather. These babies later recovered after few hours of warmth.

Neonatal Mortality

Out of 69 asphyxiated babies, 8 died reflecting an overall mortality rate of 11.5%. As the deaths occured only in severe birth asphyxia category (n=180, the mortality rate in this group was 44%. Most of the deaths occured within first 24 hours due to respiratory distress and apneic spells. Sepsis caused death after first week of age.

Discussion

The overall incidence of birth asphyxia in the present study was 4.18%. This is relatively higher as compared to 3.2% reported by Maharban Singh et al[5]. In a group of 600 high risk pregnancies monitored by Low et al the incidence of birth asphyxia was 20%[6]. Kapur et al reported birth asphyxia incidence of 6.3%[7]. The major high risk placental and neonatal factors included low placental weight, prematurity, low birth weight, male sex and acute foetal distress. Eighteen (26%) of the asphyxiated newborns showed evidence of total distress before delivery. The newborns experiencing foetal distress have more chances of developing birth asphyxia[6,8,9].

Fourteen (20%) of the asphyxiated newborns were associated with placental weight of less than 400 grams, which acts only as a contributtory factor for asphyxia neonatorum, as the actual risk factors are primarily prematurity, low birth weight and intrauterine hypoxia. This finding is in agreement with Wilson MG et al and Ronald M. Cry, who have also reported high birth asphyxia incidence in placental abnormalities like the low weight [10,11]. Seven (10%) babies with birth asphyxia were less than 37 weeks of gestation. Premature new borns are more prone to asphyxia due to their immature pulmonary status and low birth weight[1, 5]. Prematurity per se is not an isolated phenomenon but is the reflection of many complications of pregnancy like toxemia, antepartum haemorrhage and multiple pregnencies. Birth asphyxia incidence in the low weight category was 46% (n=26). Low birth weight is the final outcome of factors like maternal anaemia, prematurity, toxemia etc. Maharban Singh et al reported birth asphyxia incidence of 36.5% in preterm and 44.9% in low birth weight infants[5].

Male infants were more prone to birth asphyxia as compared to their female counterparts (ratio being 1.7:1). Although it is well known fact that females tolerate distress easily, yet relative macrosomia in males also plays an important role[5,11].

Ten (14.5%) patients of moderate to severe birth asphyxia developed septicemia. The various risk factors predisposing such babies to septicemia were low birth weight, prematurity, prolonged (obstructed) labour, forceps/Vacuum delivery. Above all, most of the asphyxiated babies, who later developed septicemia, had been referred from the peripheral hospitals. These babies had been delivered by untrained personnel after repeated unsuccessful attempts by intrumentation, making the whole process a septic one.

A variety of clinical problems were encountered following resuscitation of birth asphyxia. Respiratory failure, respiratory distress and apneic spells were accounted almost in half of the cases. Twenty (29%) asphyxiated babies developed hypothermia (core temp. <35°c). The occurrence of hypothermia can be explained on the basis of 1) patients of moderate to severe birth asxphyxia are usually in metabolic acidosis of varying degree, thereby increasing the demand for oxygen and calories and the same, if not fulfilled in time, results in hypothermia. 2) In Kashmir, this can also be attributed to cold climatic conditions. Further, the obstetric unit in Soura Institute is around one kilometer away from neonatal intensive care unit of main institution, which is further complicated by the lack of transportable incubators, leaving the tiny sick newborns to cold insult. In one earlier study. Meharban Singh etal reported hypothermia in 10.8 percent of asphyxiated new borns[5], which is also high for a prestigious centre like AIMS.

Seven (10%) patients of birth asphyxia developed convulsions which is around 10 fold more than the reported incidence of 0.2 to 1.4 percent of neonatal convulsions during first 10 days of life[13,14]. Convulsions following birth asphyxia has been variously reported to range between 4.3 to 20%[3,12], depending upon the severity of birth asphyxia. Convulsions were observed in first 24 hours in all the cases. The possible causes for convulsions being hypoxic ischemic encephalopathy, hypoglycemia and hypocalcemia. As opposed to respiratory failure, convulsions were limited solely to term babies. This finding is in agreement with observations in experimental animals that immature babies withstand hypoxia much better as compared to mature ones. Also, it has been reported that late cerebral sequelae of very severe birth asphyxia were limited to term babies.[16]

Hyperbilirubinemia developed in 10 (14.5%) of asphyxiated babies which is more than (8.6 percent) reported by Maharban Singh[5] and less than (14 percent) reported by Melteno etal[12]. Immaturity, hypoxic liver damage and subcutaneous brusing (Cephalhaematoma) accounted for hyberbilirubinemia in majoirty of cases. It has been seen that prophylactic phenobarbitone prevents the occurrence of neonatal convulsions and hyperbilibinemia offered protection against hypoxic brain damage in low birth weight newborns[17]. Three (4%) severely asphyxiated newborns developed necrotising enterocolitis. Clinical evidence of necrotising enterocolitis developed after 48 hours of life in all of them.

The overall neonatal mortality in birth asphyxia was 11.5 percent and 44 percent mortality in severe birth asphyxia is alarmingly high. In view of its potential preventability, one can hope a significant reduction in the perinatal mortality by effective monitoring of at risk foetuses during labour and prompt management of asphyxiated babies at birth. Maharban Sing etal has reported 32.6 percent mortality in severe birth asphyxia[5], Scot and Molteno etal reported 52 and 13.1 percent mortality following severe birth asphyxia respectively[12,16]. As such, asphyxiated babies must be critically monitored during the first 24 to 48 hours of life as majority of deaths occur during this period.

Respiratory failure due to lack of spontaneous breathing, respiratory distress due to in utero or at birth aspiration and apneic spells, were the leading causes of neonatal mortality. Sepsis causes deaths after 7 days of life.

The clinical evidence of foetal distress in 37 (10%) of the study group alerted to the possibility of birth asphyxia, but in others it was unexpected. This emphasizes the need for attendance of all deliveries by paediatric resident to ensure efficient resuscitation of asphyxiated babies. It also highlights the limitation of existing methods to pick up foetal asphyxia.

Note: Percentage of all the parameters in the manuscript is given in whole numbers, except for the overall incidence of birth asphyxia shown as 4.18%.

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The Editorial Board of JK-Practitioner Conveys its heart felt Condolences on the sad demise of **BEGUM AKBAR JAHAN** to:-
Dr.Farooq Abdullah
Dr.Mustafa Kamal
Dr.Mohmmad Ali Mattoo
Dr.Iftikar Ahmad
We share their grief. May God bless her.

COMPARATIVE EVALUATION OF FAMOTIDINE AND OMEPRAZOLE FOR ACID ASPIRATION PROPHYLAXIS

Mohammad Syed Qazi M.D.; Javed A. Zargar M.D.; Imtiaz A. Naqash M.D.; Mehraj-ud-Din F.F.A.R.C.S.

Abstract: *A randomized placebo controlled double blind study was conducted to evaluate the effects of Famotidine and Omeprazole on pH and volume of gastric juice in patients undergoing non-obstetric elective surgery. 150 patients of ASA Class I under study received randomly placebo or the trial drug (20 mgs of either Famotidine or Omeprazole with 10ml of water) 90 minutes before induction of anaesthesia. Gastric juice was aspirated immediately after endotracheal intubation by suction via nasogastric tube. Volume of the aspirate was measured and pH was estimated. After decoding at the end of the study the patients were grouped as Group I or placebo group, Group II or Famotidine group and Group III or Omprazole group of 50 patients each. Mean values of volume in Group 1, II and III were 25.95±10.65 ml, 8.63±2.87 and 11. 25±2.98 ml; mean pH values were 2.18±0.62, 6.70±0.47 and 4.16±0.83 in group I, II & III respectively. We found that mean volume was lower in Group II and III as compared to Group I and pH was higher in Group II and III when compared with Group I, When Group II and III were compared with Group I. When Group II and III were compared with each other, mean volume of gastric juice was less in group II as compared to group III. Similarly mean pH in Group II was higher as compared to Group III. These variations in relation to volume and pH of gastric juice in Group II and Group II and Group III were found to be statistically highly significant (p<.001). The proportion of patients considered at risk for aspiration were 36% in group I whereas no patient in group II or group III was found to be at risk for acid aspiration. We concluded that the use of Famotidine or Omeprazole is recommended before induction of anaesthesia to prevent aspiration of acid gastric contents.*

Key words: *Acid aspiration; Pretreatment; Famotidine; Omeprazole; Gastric juice; pH.*

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Pulmonary aspiration of gastric contents is a recognized hazard associated with anaesthesia in both surgical and obstetric patients. Volumes of gastric juice as little 25 ml and gastric pH levels less than 2.5 will generally produce severe pulmonary damage[1].

Preoperative use of H_2 receptor blockers has become an accepted practice as a prophylaxis against acid aspiration syndrome[2]. Famotidine is a newer H2 - receptor antagonist which is more potent than Ranitidine but with a similar durtion of action[3]. Omeprazole is a substituted benzimidazole that causes dose dependent intracellular inhibition of gastric acid secretion in humans[4]. It is a potent inhibitor of gastric acid secretion, acting as selective non competitive inhibitor of H+K/K+ ATP ase enzyme[5]. It acts directly on the parietal cell proton pump.

The present study is conducted to comparatively evaluate the effects of Famotidine and Omeprazole on pH and volume of gastric juice in patients undergoing elective surgery.

Material and Methods

This prospective double blind study included 150 ASA class-I patients undergoing various elective surgical procedures. Patients with gastrointestinal disorders and pregnancy were not included in the study. No premedication was used.

Patients under study received randomly placebo or the drug (20 mgs with 10ml of H_2O) ninety minutes before induction of anaesthesia. At the conclusion of study after decoding, patients were grouped as I (Placebo group) II (Famotidine group) and III (Omeprazole group) of 50 patients each. The placebo group acted as control.

After preoxygenation with 100% o_2 for 3 minutes all patients were anaesthetised with thiopentone sodium (5mgs/kg) and suxamethonium bromide (2mgs/kg) to facilitate smooth intubation. just after intubation a nasogastric tube was passed and gastric contents were aspirated thoroughly in the supine, right and left lateral positions. The volume of gastric contents was measured and its pH was estimated with PHM 84 research pH meter.

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Statistical analysis of data were done by using students 't' test.

Results:

There was no significant difference between patient characteristics of gender, age or weight.

Average volume of gastric juice after intubation in Group I, II, III, were 25.95±10.65 ml, 8.63±2.87 and 11.25±2.98 ml respectively as shown in table I. The variation in relation to the volume of gastric juice between Group I and Group II was statistically highly significant (p<.001). The variation in relation to the volume between group II and group III was statistically highly significant. (p<0.001) as shown in table II.

The average pH of gastric juice in placebo group was 2.18±0.62 whereas mean pH of gastric juice aspirated was 6.70±0.47 and 4.16±0.83 in group II and group III respectively as shown in table I.

The variation in relation of pH of gastric juice between group I and group II was statistically highly significant (p<.0001) where as variation in pH between Group I and Group III was also statistically highly significant (p<.001). The variation in pH between group II and group III was statistically highly significant (p<.001) as shown in table III.

Table I: Average volume (ml) & pH of gastric juice in the 3 groups

Group of cases	Volume (ml) Mean±SD	pH Mean±SD
Group I (Control)	29.95±10.65	2.18±0.62
Group II (Famotidine)	8.63±2.87	6.70±0.47
Group III (Omeprazole)	11.25±2.98	4.16±0.83

Table-II: Statistical comparision of volume of gastric juice between Group II and Group III

Group II Vol (ml) Mean±Sd	Group III Vol (ml) Mean±SD	Difference in Mean±SD	1 value	p value	Remarks
8.63±2.87	11.25±2/98	2.62	4.44	<0.001	Highly significant

Table-III: Statistical comparison of pH of gastric juice between Group II and Group III

Group II Vol (ml) Mean±Sd	Group III Vol (ml) Mean±SD	Difference in Mean±SD	1 value	p value	Remarks
6.70±0.47	4.16±0.83	2.54	19.54	<.001	Highly significant

The incidence of high risk case (pH < 2.5 and vol. > 25ml) was 36% in Group I (n=18) whereas in group II and Group III the risk was nil.

Discussion:

When associated with anaesthesia pulmonary damage due to aspiration of the acidic contents of the stomach is thought to be reliably prevented by increasing gastric pH above 2.5 and reducing the volume of stomach contents below 25 ml[6]. However, it is not correct to assume that gastric fluid with a pH above 2.5 if aspirated will prove harmless, as apiration pneumonitis has been described following inhalation of fluid with pH of 3.5.

In the present study the mean volume of gastric juice in group II was 8.63 ml as compared to control group (25.95ml). Similarly mean pH of gastric juice was higher in group II (6.70) as compared to pH of 2.18 in placebo group I. These variations were statistically highly significant when compared with group -I (p<.001). This showed that famotidine given in dose of 20mgs orally 90 minutes before induction of anaesthesia was effective in reducing the volume and raising the pH of gastric juice to safer levels at the time of intubation. Our results are in accordance with the findings of Escolano F, et al (1989), Kazuo Abe et al (1989) and Taneja Sanjay, et al (1992)[6,7,8] as shown in Table IV.

Table-IV: Mean volume & pH of gastric juice in different studies with 20 mg of Famotidine given 90-120 minutes before Induction of Anaesthesia.

	Study	Volume (ml)	pH
1.	Escolano et al 1989	5.4	7.4
2.	Kazuo Abe et al 1989	8.7	6.2
3.	Sanjay Taneja	9.63	7.03
4.	Present study	8.63	6.70

In group-III, the mean volume of gastric juice was 11.25 ml which was less as compared to 25.95 ml in control. Similarly the mean pH in group III was 4.16 as compared to 2.18 in control group. The variations in relation to the pH and volume of gastric juice between group III and I were statistically highly significant. From these observations it was obvious that Omeprazole is also effective in reducing the volume and raising the pH of gastric juice to safer levels when compared to control group. Our results are comparable with Moore J, et al (1989), Gin T, et al (1990), Ewart MC et al (1990), Atanossoff et al (1992) and Hendolin et al (1993)[9,10,11].

When group-II and III were compared to each other, it was found that the mean volume of gastric juice was less in Famotidine group (8.63ml) as compared to Omeprazole group (11.25ml). Similarly mean pH in group-II was found to be on higher side (6.70) as compared to group-III (pH-4.16). These variations in volume and pH between these groups were found to be statistically highly significant. Although both famotidine and Omeprazole were found to raise gastric pH and decreased gastric volume to safer levels. Yet the decreased effect of Omeprazole as compared to Famotidine could be attributed to lower dosage of Omeprazole (20mgs) used in this study. In all other previous studies higher dosage of Omeprazole (40 to 80 mgs) have been used either once or twice before induction of anaesthesia.

While studying the patients at high risk for aspriation, it was found that 36% of patients in group I were at higher risk for acid aspiration syndrome while no patient in Group II or Group III was found to be at risk for acid aspiration syndrome. In other words both Famotidine and Omeprazole gave 100% protection against acid aspiration as compared to control group where only 64% of the total cases were protected.

In conclusion our study demonstrated that famotidine 20mgs and Omeprazole (20mgs) are highly effective in raising pH of gastric juice above 2.5 and lowering volume of gastric juice below 25 ml when given 90 minutes before induction of anaesthesia and also Famotidine 20mg is superior to Omeprazole 20mgs given orally 90 minutes before induction of anaesthesia.

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TANGENTIAL FIELD TREATMENT OF SUPERFICIAL TUMOURS WITH CO-60

W.H.Andrabi; S.K.Koul; S.M.Abbass; M.A.Bhat; M.A.Ashraf

Abstract: Treatment of superficial tumours with Co-60 poses lot of difficulties because of inherent nature of Co-60 beams, its housing , small field sizes, difficulty in dosimetry, positioning and reproducibility.

Presented in this paper are planning details of a patient with squamous cell carcinoma of lip for parallel and opposite tangential field treatment using Co-60, Theratron-780.

Key words: Superficial Tumours; Cobatt-60; Theratron-780

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INTRODUCTION

Incidence of skin tumours in our valley is on an increase and Radiotherapy management of these tumours especially at sites like face, scalp and abdominal wall poses many clinical and technical problems [1-4].

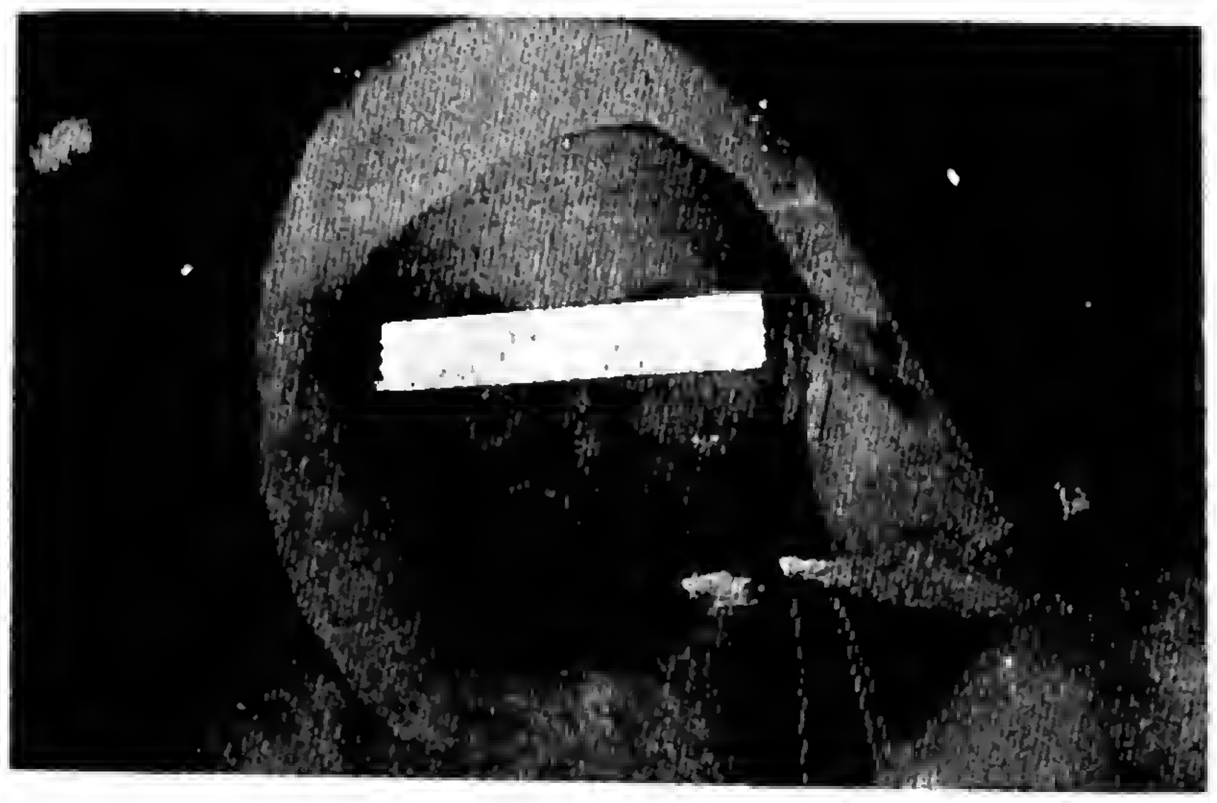


Fig.I Field markings on the treatment

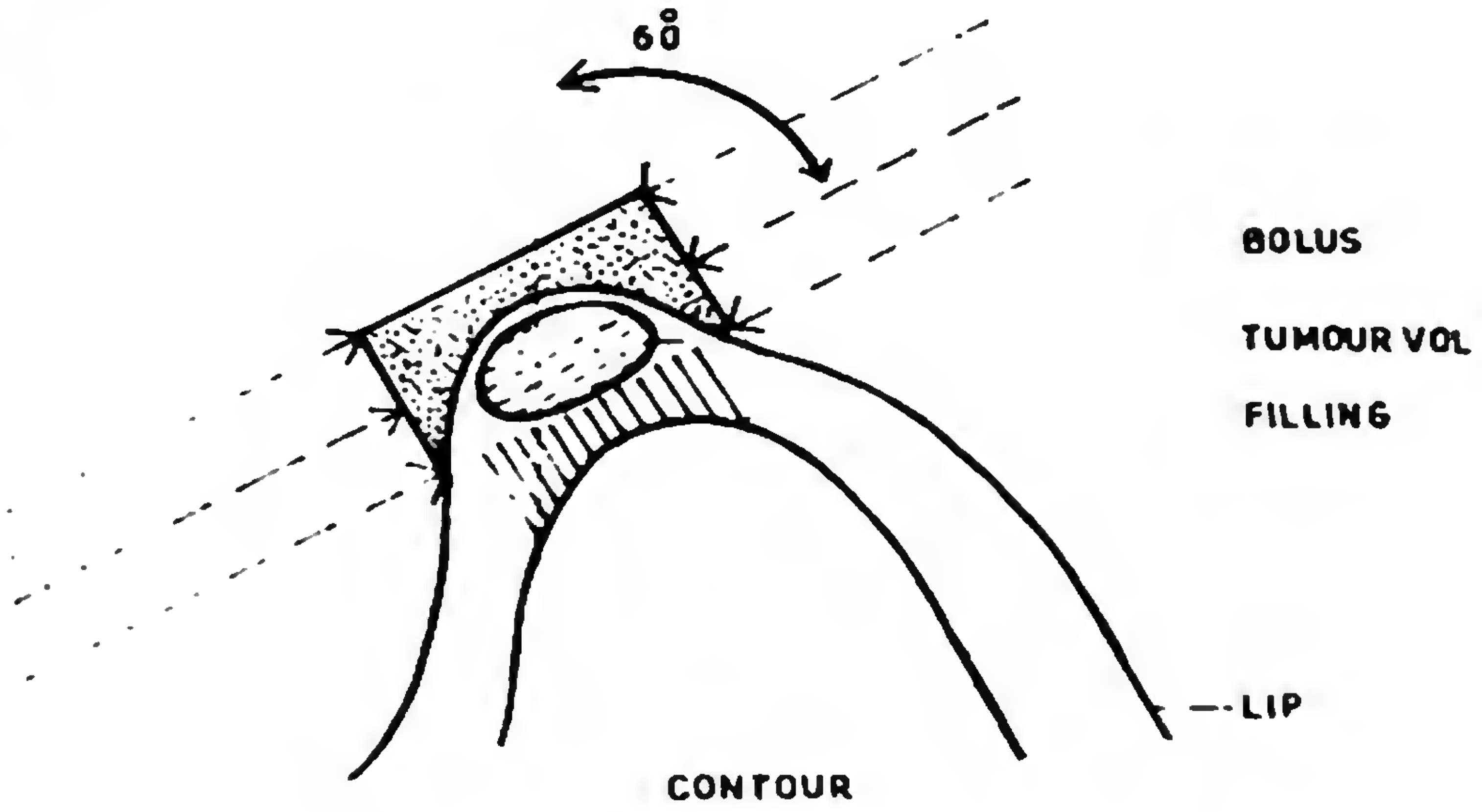
Besides surgery, most of these patients need postoperative radiotherapy[(2)]. Though radiotherapy with electrons/ superficial therapy, is ideal for treating such lesions, many centres in our country don't possess these facilities. As a result most often treatment with Co-60 beam/beams is the only choice for treatment of these lesions. However, there are many difficulties in execution of treatment by this procedure viz., dosimetry of prescribed small field sizes, irregular and curved lesion sites, dedicated beam geometry, reproducibility and immobilization. In our centre we have successfully treated number of patients with Co-60 using parallel and opposite tangential fields.

Presented in this paper is the radiotherapy planning details of one of our patients with squamous cell carcinoma of lip using tangential fields. We hope that centres with Cobalt-60 units will utilize this technique for the benefit of such patients.

MATERIAL AND METHODS

Fifty five year old patient with squamous cell carcinoma on right side of lower lip excised a month back reported for postoperative radiotherapy (p-1). Direct Co-60 field to the lesion would obviously irradiate the whole mouth, mucosa and underlying tissues resulting in adverse reactions. Tangential field treatment was thus chosen.

Smallest field size available on Theratron-780. i.e.,4 x 3 cms^2 was used. Field size and centre was marked by Radiation Oncologist for SAD technique for easy execution treatment.



THE TREATMENT PLAN

Filling was introduced in the gap between the lip, the

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teeth and gingiva to make the lip flat and bulge outward (Fig.1) Wet cotton was used as bolus over the scar to compensate for the missing tissue and ensure proper contact. Proper neck rest was used for immobilisation and reproducibility.

Contour of the patient was taken by an isocentric machine. Gantry angles for medical tangential (60⁰) and lateral tangential (24O⁰) were used to achieve parallel and opposite field treatment. Dosimetry was done in identical conditions, keeping 0.6 cc chamber (2581 Nuclear Enterprises-NE) between perspex sheets of equivalent thickness. Secondary standard dosimeter Farmer 2570 (NE) was used for measurement.

A dose of 50 Gy in 25 equal fractions in five weeks was delivered.

RESULT AND DISCUSSION

Treatment was executed smoothly, Underlying tissues of the mouth were spared from un-necessary exposure. Thus, adverse reaction in the mouth were completely avoided.

Patient is on regular follow up and is doing well with disease free status. The results are comparable with treatments using either superficial therapy or electrons.

We believe that patients who have no access to electron therapy can be treated by C0-60 tangential beams with proper dosimetry and setup. We have treated good number of patients successfully till date by this technique and recommend use of this method for treatment of such lesions when other modalities are not available.

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CONFERENCE NOTICES

- **The 6th.Asian Pacific American gastroenterological Conference and the 41th. Annual Conference of the Indian Society of Gastroenterology will be held in New Delhi on November 19-25 2000.**
  For details please visit website www.isgcon2000.com or contact Dr.Rakesh K Tondon,Organizing Secretary,Deptt.of Gastroenterology,All India Institute of Medical Sciences, New Delhi-110129.
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- **International Summit on Coronary Artery Disease in the New Millennium,Mumbai,Maharashtra 15-18 February 2001**.For details contact:-Dr.Satyavan Sharma,Secretary General,Academy of cardiology,75th,tth floor,Lady ratan Tata Centre,Maharshi Karve Road,Cooperage,Mumbai 400021,Maharashtra,India.

- **Third International workshop on Advanced Therapeutic Endoscopy and National conference of Society of Gastrointestinal Endoscopy of India,Mumbai,Maharashtra 3-6 February 2001**.
  For Details:-Amit maydeo,Digestive Disease Centre,Bhatia General Hospital,Tardeo,Tardeo road Road,Mumbai 400007

HEPATOCELLULAR CARCINOMA IN AN ECTOPIC ACCESSORY LOBE OF THE LIVER A CASE REPORT AND REVIEW OF LITERATURE

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Abstract: The occurrence of accessory livers is known but very rare. Complications like torsion, infarction and cirrhosis have been described previously[1,2,3]*, metastatic carcinoma in ectopic liver tissue has also been reported*[4] *A primary tumour in an ectopic liver tissue has not been reported till date. We report a case of hepatocellular carcinoma in an ectopic accessory liver tissue in a new born baby with omphalocele.*

Key words: Hepatocellular carcinoma, Omphalocele, Accessory liver, Ectopic liver.

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Introduction

The presence of an accessory lobe of liver in association with abdominal wall defects has been described previously[3]. Although uncommon, ectopic liver tissues have been found in various sites including the left triangular ligament of liver, the spleen, the umblical fossa, the omentum, the retroperitonium, near the celiac axis, the gall bladder and its vicinity and the lungs[1,5,6,7]. Usually these are enountered as an incidental findings. 20-50% cases of omphaloceles contain liver tissue as a content suggesting the possibility of a portion of developing liver being trapped in the narrowing umbilical ring[8,9,10]. Surgical repair of omphalocele may at times necessitate resection of a part of liver or excision of an accessory lobe[11]. Accessory lobes of liver have undergone torsion and infarction requiring surgical intervention[2,3]. Cirrhosis has been reported in ectopic liver tissue[1] as well as in the pedunculated accessory lobe. Accessory lobes have been incriminiated in the development of extrahepatic portal hypertension by exerting pressure on portal vein during development[12]. Metastatic tumour has also been reported in ectopic liver tissue[4]. A primary tumour in accessory or ectopic liver tissue has, however, not been described in literature till date. Here a case of primary hepatocellular carcinoma in an ectopic accessory lobe of liver occupying the omphalocele sac of a new born baby is presented along with review of the literature.

Case Report

A male baby was referred to the department of Paediatric Surgery of Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar soon after delivery with a moderate sized omphalocele. He was the product of a full term normal delivery and a consanguineous marriage. He was fifth in birth order and other siblings (3 females and one male) were normal. He had passed urine and stool soon after birth. Baby had been fed a couple of times and had tolerated the feeds. He was 3.25 kg in weight, active, pink, with a heart rate of 110/minute and respiratory rate of 24/minute. The detailed examination of cardiovascular, respiratory and nervous system was essentially normal. Abdominal examination revealed an omphalocele 5cm x 7 cm size. It was encircled by about a 2cm wide rim of skin and the rest was covered by a membrane through which bowel loops could be seen. The umbilical cord was attached to the inferior surfacer of the sac. Genitalia and perineum were normal.

Investigations revealed a haemoglobin level of 17.2gm, TLC 9.0 x 10^9/L, DLC 70%, polymorphs and 30% lymphocytes. The platelet count was 152 x 10^9/L, bleeding time was 3 minutes and clotting time 5 minutes and 45 seconds. Blood urea, serum creatinine, serum electrolytes were normal. Liver function tests, blood sugar and routine urine examination were normal. Blood group was B-positive. X-ray chest was unremarkable. X-ray abdomen showed a rounded homogeneous opacity in central abdomen. Gas distribution in the bowel was satisfactory and no other abnormal finding was observed. The baby was nursed in an incubator. He was put on nil by mouth, nasogastric suction, intravenous fluid and prohylactic antibiotics (Ampicillin, Gentamycin and Metronidazole) were started. 150ml of blood were cross matched.

Following morning, the patient was subjected to surgery under general anesthesia. The omphalocele was opened by making a circumferential incision and contained bowel loops and a small pink fleshy mass. Bowel loops

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were separated from the sac. Before reducing the contents, the diaphragm, the duodenum, small and large bowel and other viscera were examined thoroughly. Few adhesions observed in the herniated bowel loops were lysed. There was evidence of malrotation in bowel with few Ladd's bands. These were lysed and the mesentry was widened. The liver and the spleen were normal in place and appearance. The pinkish fleshy nodule measured 4cm x 4.5cm in size and was seen dangling amongst the herniated bowel loops. This had the colour and consistency of liver. The normal liver was at its appropriate place in right upper abdomen and no abnormality was observed in its gross appearance. The fleshy nodule was freely mobile and had a long tiny pedicle growing towards the porta hepatis. After a lot of consideration it was decided to remove this nodule to guard against the possibility of undergoing torsion and infarction following surgery.

Hence the pedicle was ligated deeply near the porta and the mass excised and sent for histopathological examination. The abdomen of the baby was closed. Muscular layer needed little streching, skin however was approximated with slight tension. Umbilicus was fashioned. The closure was achieved without much difficulty, after removing the fleshy nodule referred to above. Post operatively the patient was continued in an incubator and was put on nasogastric suction, antibiotics and IV fluids. Oral feeds were started on 5th day when bowel sounds and bowel movement were statisfactory. Antibiotics were given for seven days and sutures were removed on the tenth post-operative day. The post-operative period was relatively uneventful. The biopsy report showed the presence of hepatocellular carcinoma in the fleshy nodule removed at the operation. On receiving this report the patient was subjected to repeat investigation which included the haemogram, liver function tests, alpha fetoproteins, ultra sound abdomen especially to scan the liver, porta hepatis and caeliac area, x-ray chest and renal function tests. All of them were unremarkable. The child had a smooth recovery and after thorough discussion with the neonatology and oncology colleagues, the patient was allowed home two weeks after surgery. The parents were explained the situation and directed to attend the follow up clinics at regular intervals. The patient has now been followed up for over three years. His general condition, growth and development has been normal. Follow up haemogram, liver function tests, alpha fetoproteins, x-ray chest, ultra sound examination of the abdomen performed at regular three monthly intervals have been normal. We feel the child has been cured and there is no evidence of residual tumour.

Discussion

Anomalies of liver are uncommon and for the most part consist of variations in the size and configuration of the true right and left lobes[2] Accessory lobes may also occur[13].

The term accessory liver should not be confused with multiple lobes of liver in which there are deep external clefts grossly dividing the liver into lobes. The accessory liver grossly apears as either a detached structure or a small organ attached by fibrous tissue to the main liver[14]. According to their anatomical relations three different types of accessory livers are recognized.[3,12]

Type-I: The separate accessory lobe duct drains into an intra hepatic duct of the normal liver.

Type-II: The separate accessory lobe duct drains into an extra hepatic bile duct of normal liver.

Type-III: The accessory lobe is incorporated in a common capsule with normal liver. The bile duct of accessory lobe drains into an extra hepatic duct.

Ectopic liver tissue, in some instances, may represent an accessory lobe whose pedicle attaching it to the main body of the liver has atrophied and cannot be identified. Such tissue may also arise from pleuri potential forgut tissue developing as liver in other visceral organs[15]. Presence of ectopic liver tissue has been reported previously on the gall bladder[1] suspensory ligament[5], umbilicus[6] and lungs[7]. These have usually been incidental finding with no clinical importance. Presence of liver tissue in the omphalocele sac is not unusual. Liver tissue is present in 20-50% omphaloceles and at times this organ constitutes the main problem in repair. The spectrum of liver tissue in the omphalocele varies from total herniation of liver to the presence of a small ectopic nodule[3,5,8,10,16,17]. Accessory hepatic lobes are usually asymptomatic and as a rule they need not be removed[2]. On rare occasions they undergo changes that produce symptoms and even require surgical correction. Cullen[5] reported successful excision of an accessory lobe of liver that had undergone torsion and gangrene. Levi et al[18] removed an accessory lobe presenting as an ischemic mass in the lower abdomen thought preoperaively to be a tubo-ovarian mass or appendiceal abscess. Nora and Carr[6] reported a case of umbilical accessory liver which resembled in its features to our case. Accessory lobes has presented as torsion with partial colonic obstruction[19], torsion of gall baldder embedded in accessory lobe[20], and also as extra hepatic portal hypertension by causing congenital obsruction of the portal vein[12]. Accessory lobes have undergone Cirrhosis[1] and have been the seat of metastatic tumour[1]

Torsion of accessory lobe has also been reported by Watson and Lee[2], Elmasalma et al[3] and others. However, the presence of a primary malignancy in an accessory lobe of ectopic liver tissue has not been reported. The histopathological examination of the accessory lobe removed in the present case revealed the presence of hepatocellular carcinoma which to our knowledge is the first observation of its type. Hepatocellular carcinoma is rare in children under 3 years of age[21] and its presence in a new born adds to the significance of this report. We therefore recommend that accessory lobes, whenever encountered, should be excised if their pedicle is long and narrow. This is the only way to prevent them from torsion and infarction and to avoid subsequent diagnostic difficulties as a result of their a typical presentation.

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AGGRESSIVE ANGIOMYXOMA - REPORT OF THREE CASES AND REVIEW OF LITERATURE

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***Abstract:** Aggressive angiomyxoma (AA) is a rare benign mesenchymal tumour. The prefix "aggressive" is used to denote the locally infiltrative nature of this tumour. It has predilection for female pelvic and perineal regions. We report clinicopathological findings of three cases of aggressive angiomyxoma. All the three patients were females ranging in age from 22-35 years, with involvement of vulva and perineum. All the tumours were less than 7 cms in size and were locally excised. At the end of 6 months of follow up, no local recurrence or distant metastasis was seen. Histologically, the tumors were sparsely cellular consisting of benign stellate and spindle shaped cells embedded in a myxoid stroma Mitotic index was 1-2 / 10 HPF. The tumour matrix showed positivity for mucosubstances. We, conclude that AA is a benign mesenchymal tumour occuring in young females of reproductive age group and is quite site specific. Long term follow up is necessary for documenting any local recurrence/metastasis.*

***Key words:** Aggressive angiomyxoma (AA), mesenchymal tumour.*

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Introduction:

Steeper and Rosai were the first who reported an uncommon mesenchymal tumour which was locally infiltrative and commonly involved the perineal region and pelvis in adult females[1]. However, cases of aggressive angiomyxoma have also been reported in male patients[2,3]. So far, 55 cases of aggressive angiomyxoma have been reported in the world literature with female to male ratio of 5:1. The present study reports clinicopathological findings from 3 cases of aggressive angiomyxoma.

Material and Methods

Hematoxylin and eosin stained slides from all three cases were reviewed. Special stains like Alcian Blue at PH2.5 and Mucicarmine were also performed. The mitotic counts were evaluated by examining 10 random high power fields (40x). only those areas of the tumour which were highly cellular were examined for mitotic figures.

Results

Clinical Picture: The clinical findings of all the cases are listed in table-I. All the three patients were females ranging in age from 21-35 years at the initial presentation.

The site of involvement was perineal region in all the cases. All the patients were aware of a mass in perineal region and had compliants of pain in perineal and labial areas along with a sensation of heaviness. Preoperative diagnosis were labial cyst (inclusion Cyst). Lipoma and Bartholin's cyst. All the patients had local excision of their tumour. At the end of 6 months of follow up, all of them were alright without any evidence of recurrence or metastasis.

Table I

S. No.	Age & Sex	Location	Size	Duration of sumptoms	Preoperative diagnosis	Surgical removal
1.	22 years/F	Vulva (right Labia)	4cms	6 years	Labialcyst ?Inclusion cyst.	Local Excision
2.	26 years/F	Vulva (Left Labia)	6cms	4 years	Lipoma	Local Excision
3.	35 years/F	Bartholins Gland region	6.5cms	3 1/2 years	Bartholins Cyst	Local Excision

Pathological Findings

Grossly all the tumours varied from 4 to 6.5 cms in diameter and showed smooth external appearance, cut section were soft to firm and gelatinous/myxoid in appearance. A few areas of hemorrhage were also noticed. In all the three cases, the tumors were well encapsulated.

Microscopically, at low power, the tumors were composed of uniformally scattered spindle and stellate shapped cells in a loose firbromyxoid stroma (Fig 1). The stroma consisted of numerous scattered bloodvessels of varriable sizes. An increased cellularity of the tumour cells was noticed around the blood vessels at certain foci (Fig. 2). The individual tumour cells were stellate shaped with scant amount of cytoplasm, had bland nuclei with granular chromatin. Blood vessels showed normal endothelial lining. At fews places, extravasated RBC's were also noticed in the stroma. Mitotic count varied from 1-3

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mitotic figures/10 HPF. No abnormal mitotic figures were seen. When subjected to special staining, the myxoid stroma was found positive for Alcian Blue at PH2.5 only one case showed focal positivety for mucicarmine.

Discussion:

Aggressive angiomyxoma is an uncommon but distinct mesenchymal tumour which commonly involves the soft tissue of pelvis, especially the vulva. It is commonly seen in females though some cases of this neoplasm have been reported in males also, where it is generally seen in the scrotal sac[2,3,5]. Since, the categorisation of this tumour as a distinct entity by Steeper and Rosai in 1983, less than 60 cases have been reported in the literature. More than 75% of cases occur in females in reproductive age group[1,2]. These tumours are commonly mistaken as Bartholin's cyst or as an inclusion cyst in our study all the three patients were in the younger age group (2-35 years) without any micro scopic evidence of infiltration into the surrounding tissues. At the end of six months of follow up, no evidence of recurrence at the local site or metastasis to distant site was noticed. The low recurrence rate could be attributed to the low mitotic division of these tumours. In the earlier studies also, the documentation of clinical recurrence has been as late as 14 years after the initial surgery[1]. This, perhaps suggested that angiomyxoma is a very slow growing tumour and hence a long term follow up is required before the possibility of recurrence can be negated. As far as histogenesis of this tumour is concerned, it is highly debatable. Some workers have favoured a derivation from the stromal cells, unique to the perineal region, where they express fibroblastic and myofibroblastic features[1]. An other group of workers have shown reactivity for Desmin and muscle specific actins in the tumour cells, there by suggesting myogenic derivation of the tumour cells[6].

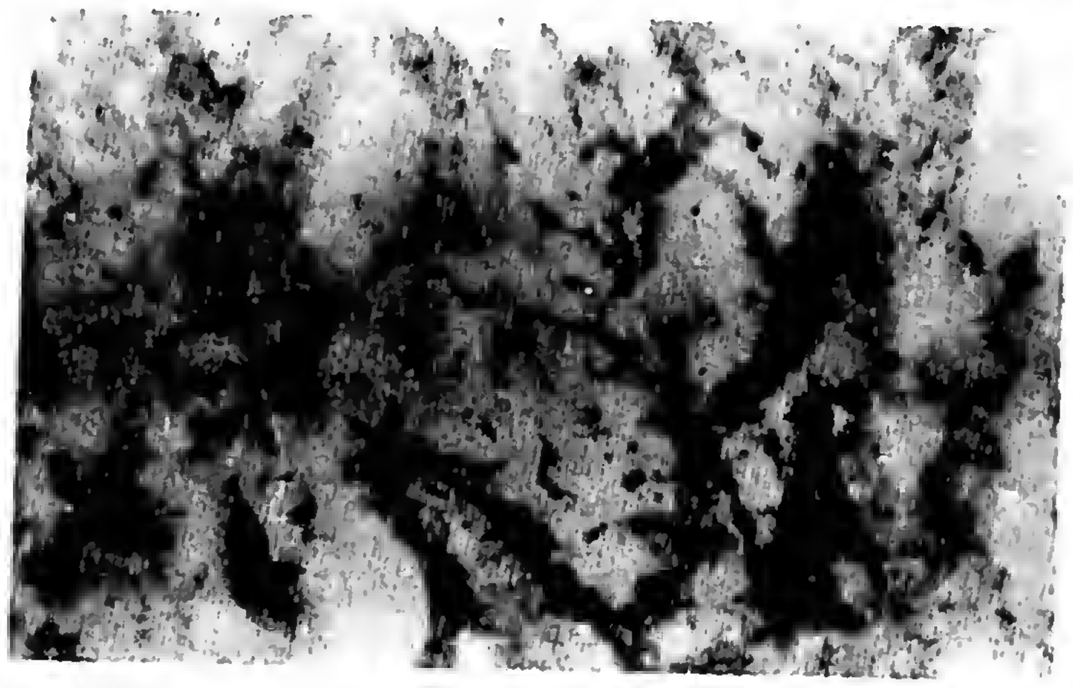
Fig. I. Photomicrograph showing spindle and stellate shaped cells in fibromyxoid (4OX)

The Differential diagnosis of angiomyxoma includes various benign and malignant lesions[6]. Amongst the benign lesions, superficial angiomyxoma is a rare, small tumour which occurs primarily in the dermis and consists of abundant mucin rich matrix and has a sparse population of stellate cells. The degree of vascular prolifertion as seen in angiomyxoma is absent in superficial angiomyxoma[7]. Angiomyofibroblastoma is a newly described entity seen in vulva, vagina and sometimes in the scrotal sac[8]. It is characterized by extreme degree of vascular proliferation, minimal stomal mucins and larger stromal cells resembling plasmacytoid hyaline cells admixed with multinucleated gaint cells. Soft tissue myxomas are very rare in pelvic and perineal regions and microscopically they are less cellular and contain few blood vessels. The malignant tumours which closely resemble angiomyxoma are myxoid type of malignant fibrous histiocytoma (MFH), liposarcomas and leiomyosarcomas. Hence, for a definitive histological diagnosis of angiomyxoma, an adequate sampling along with relevant clinical findings is must. Though, benign in nature, the angiomyxomas have a tendency for local recurrence if not excised properly. Thus, a long term follow up is necessary.

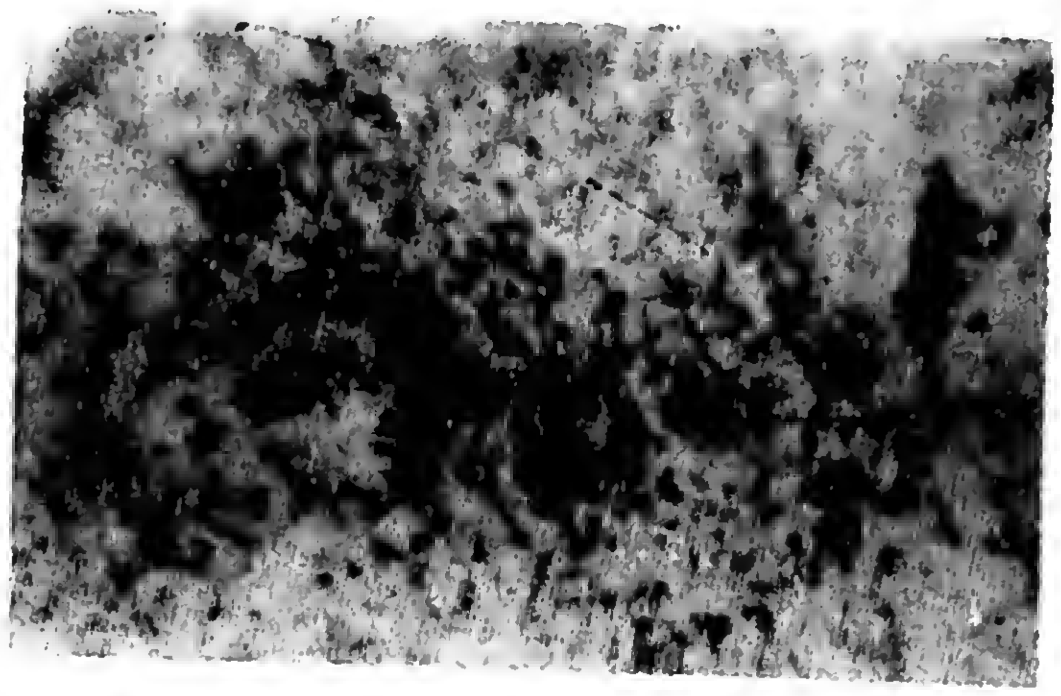
Fig. II. Photomicrograph showing prominant blood vessels surrounded by tumor (4OX)

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SPIGELIAN HERNIA

K.S. Metha M.S.; Imtiaz Shah M.S.

Abstract: Spigelian or lateral ventral wall hernia occurs infrequently. The sign and symptoms of the Hernia are not characteristic in common, these hernias give rise to intestinal obstruction. Surgical repair is mandatory because of the fairly high incidence of strangulation.

Key words: Hernia, Rectus, Spigelian, Ileum.

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Introduction

Hernia of the semilunar line or spigelian hernia is uncommon. It's true incidence is probably greater than the relatively small number of patient reported within literature, due to failure to diagnose at the earliest. About 200 cases have been reported in the world Medical Literature and most of these case reports come from Foreign countries.

Case Reports:

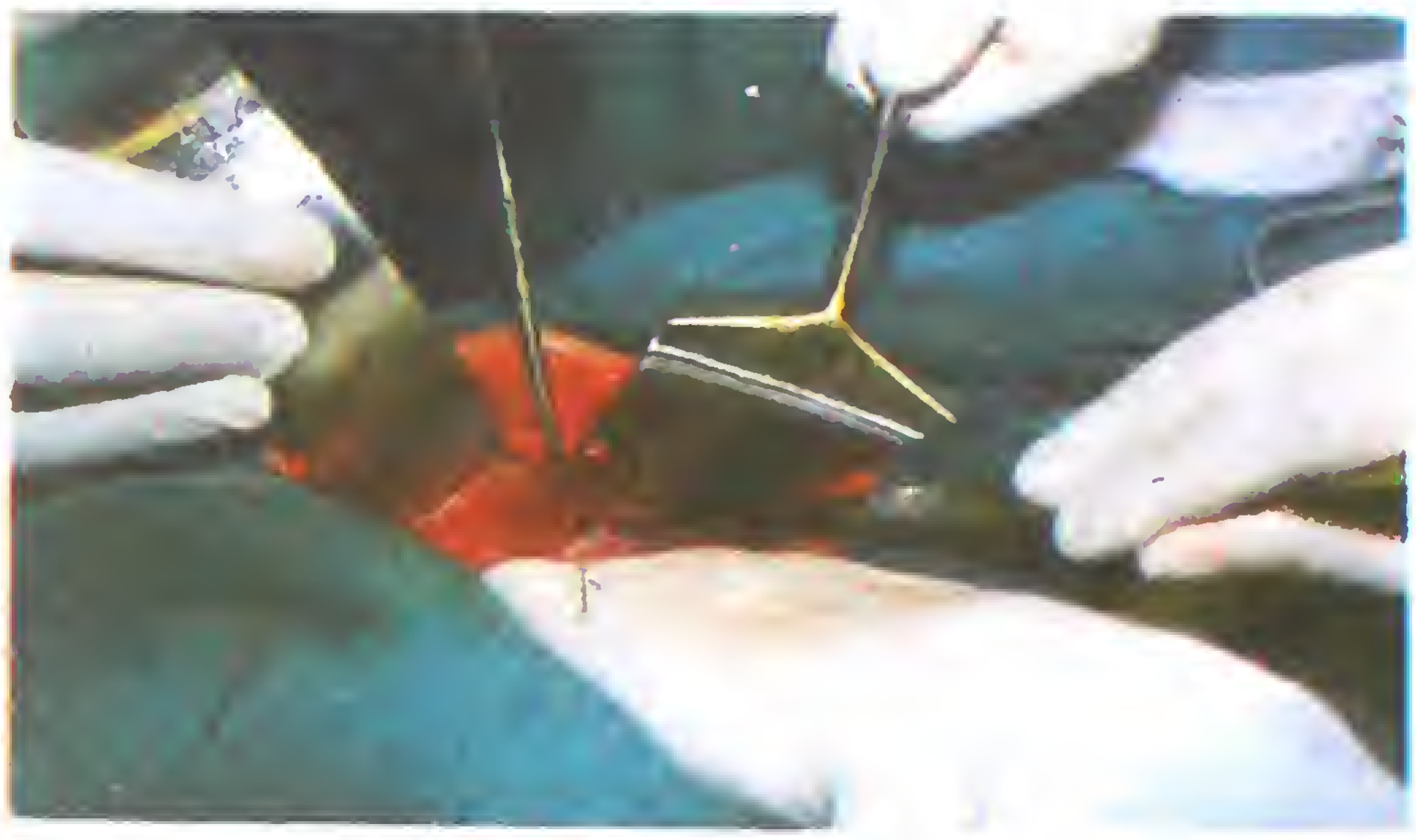
A 60 years old man, known hypertensive and chronic smoker, presented in the Emergency Ward with a hard swelling on the left side of the abdomen associated with pain and vomiting for the last one day. There symptoms were preceeded with gradual distension of the abdomen, followed by constipation.

On clinical evaluation, the patient was in severe pain abdomen with distension, with a B.P. of 210/130 mmHg. of mercury. There was a firm oval swelling (2cm x 1.5 cm) fixed, non reducible, palpable adjacent to the lateral wall of the left rectus, with no impulse on coughing and with exaggerated bowel sounds on auscultation. Routine lab investigations like CBC, Renal parameters, Electrolytes were within normal limits. X-ray abdomen revealed dilated loops.of small intestine with multiple air fluid levels. Ultra sound abdomen was inconclusive and the patient was provisionally diagnosed as intestinal obstruction ilio-ilial intussuption. The patient was put on I/V fluids and drip suction. But the patients condition deteriorated and decision for laparotmy was made.

After putting the patient to sleep under Nitrous oxide and halothane, with all asceptic precautions abdomen was opened by left lower pramedian incision. A segment of ileum was found to be stuck to the anterior abdominal wall just lateral to the left recuts, which had protruded through the defect in the semilunar line. Proximal gut was dilated and the distal loop was shrunken. Half of the circumference of the distal ileum had herniated within a defect of about 3cm x 2cm. With a gentle traction on the loop the hernia was reduced and peritoneal defect was repaired with 2° vicryl and sheath with 2° prolene. The patient had an uneventful recovery and was discharged on 10th post operative day.

Discussion

The world literature contains references to over 200 cases of herniation occuring at the lateral margin of the rectus muscle, without any history of previous trauma. Protrusion of a sac of peritonium, organ or preperitonial fat from its normal position through a congenital or acquired defect in the spigelian fascia is referred to as "Hernia Spigeli". The term spigelian hernia usually refers to hernia located above the inferior epigastric vessels. These hernias are usually difficult to palpate and have often been called occult or masked hernia. The condition



Photograph showing defect in the semilunar line left side (Spigelian Hernia)

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arises spontaneously and is seen mainly in old age group and occurs typically in obsese individuals who have lost considerble weight due to dieting or disease. The importance of considering this diagnosis is emphasized when we realise that many of patients are thought to have functional disease and later on present with incarceration, strangulation and intestinal obstruction and too often the patient proves that our original impression was wrong.

The hypothesis which appears to fit best the observation made during operation is that of Zimmerman, Anson, Morgan and Mcvay[6]. These authors have presented anatomical evidence that spigelian hernia occurs because of weakness developed within the transversus and internal oblique muscle layers. Fat plays its part by first infiltrating and then weakening the internal oblique and then acting as leading wedge for herniation.

These conclusion are in agreement with those of Bailey, D[1], who has recently reviewed the subject and who commented that this type of hernia is not as rare as it was once thought to be.

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"DELAYED PRESENTATION OF POST-TRAUMATIC DIAPHRAGMATIC HERNIA"

J.N. Karbhase; Rajendra Umbarkar; Javed Khan;

***Abstract:** Though diaphragmatic rupture following penetrating trauma is not uncommon, delayed presentation nearly after 20 years is rarity. The possibility of such a diagnosis should be born in mind in a patient with chest and abdominal discomfort particularly because not all patients will volunteer the history of traumatic injury in the past. Thoracic approach is mandatory in delayed herniation as invariably, there are adhesions between the bowel and the pleural cavity. Additional exposure through the abdomen was required in this case because of difficulty in reducing the herniated bowel. It is safer to use a prolene mesh or fascia lata if the edges of the ruptured diaphragm are not approximating easily. Reactionary pleural effusion can give some degree of morbidity. However, the end result is invariably satisfactory.*

***Key words:** Diaphragmatic herma, Pentrating injury.*

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Introduction

The traumatic diaphragmatic hernias are frequently associated with injuries of either chest or abdominal organs. Because of this, the immediate mortality of traumatic diaphragmatic hernias is high.

It is rare to have a traumatic diaphragimatic hernia and patient remaining sympton free for a long time. These patients usually present to clinicians either as accidental findings, abdominal or chest symptoms or signs of acute intestinal obstruction. With this kind of delayed presentation, the trauma which is the cause of this hernia many a times is forgotten by the patient. Thus, the management of such patients requires careful history, examination and possibility of the traumatic hernia are essential for the successful management.

Case Report We are herein presenting a patient who had traumatic diaphragmatic rupture and presented to us after 20 yrs. following injury.

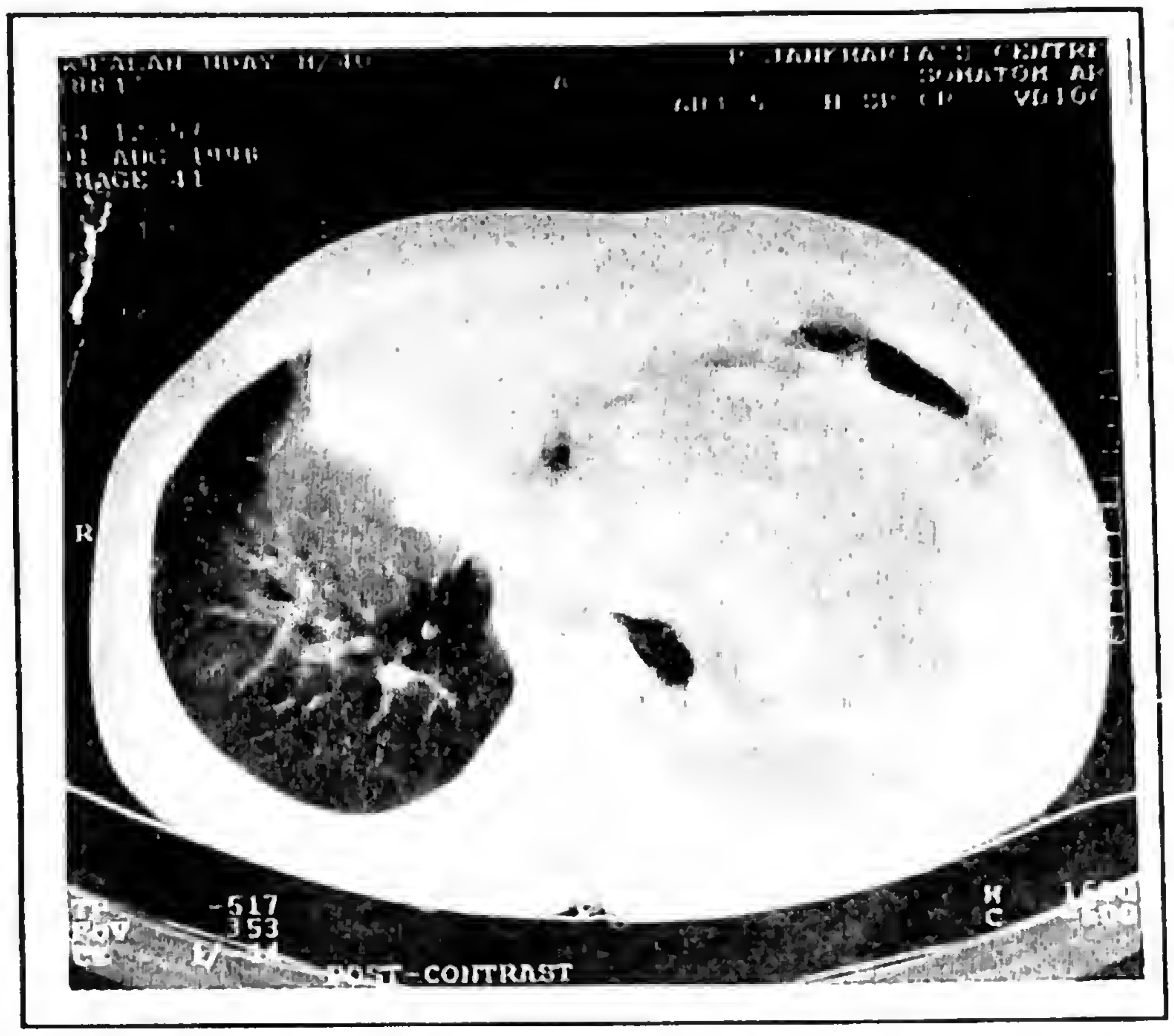

Fig. 1

A 40 yrs., old male, chronic smoker, chronic alcoholic, site supervisor by profession was admitted with complaints of dyspnoea on exertion, eructations and gaseous distention of stomach of four years duration. Patient had sustained chest trauma 20 yrs. ago and inconclusive needle aspiration was done from left pleural cavity. Examination revealed a pulse rate of 88/mt. BP: 140/90 mmHg. Air entry was decreased in the left lower zone of chest. Rest of the physical examination was normal. Haematological and biochemical investigations were within normal limits. X-ray chest PA view (Fig. I) showed homogenous opacity in the left lower zone. C.T. Scan of the thorax showed bowel loops in the left side of the chest cavity (Fig II). Pulmonary function tests revealed predominant restrictive low F.V.C. The diagnosis of delayed presentation of traumatic diaphragmatic rupture on the (L) side was obvious on reviewing the investigations.

The diaphragm was explored by a left lateral thoracotomy incision through 6th intercostal space and care was taken not to injure the bowel while opening the pleural cavity. There were adhesions between the bowel and mediastinal pleura which were released by sharp

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dissection. Abdominal contents were partially reduced and reduction was completed by opening the abdomen through an upper midline incision. The left lower lobe of lung was collapsed. The diaphragmatic defect about 6 cm x 6cms on the left side was identified and edges demarcated. The defect was closed with 2-0 exhibond sutures using a prolene mesh.

Lung was expanded, a thoracic drain kept and thoracotomy and abdominal wounds closed back. The post operative course was uneventful except for the fact that the intercostal drain continued to drain serous discharge for 20 days. The patient was discharged on the 20th day when the drain was removed.

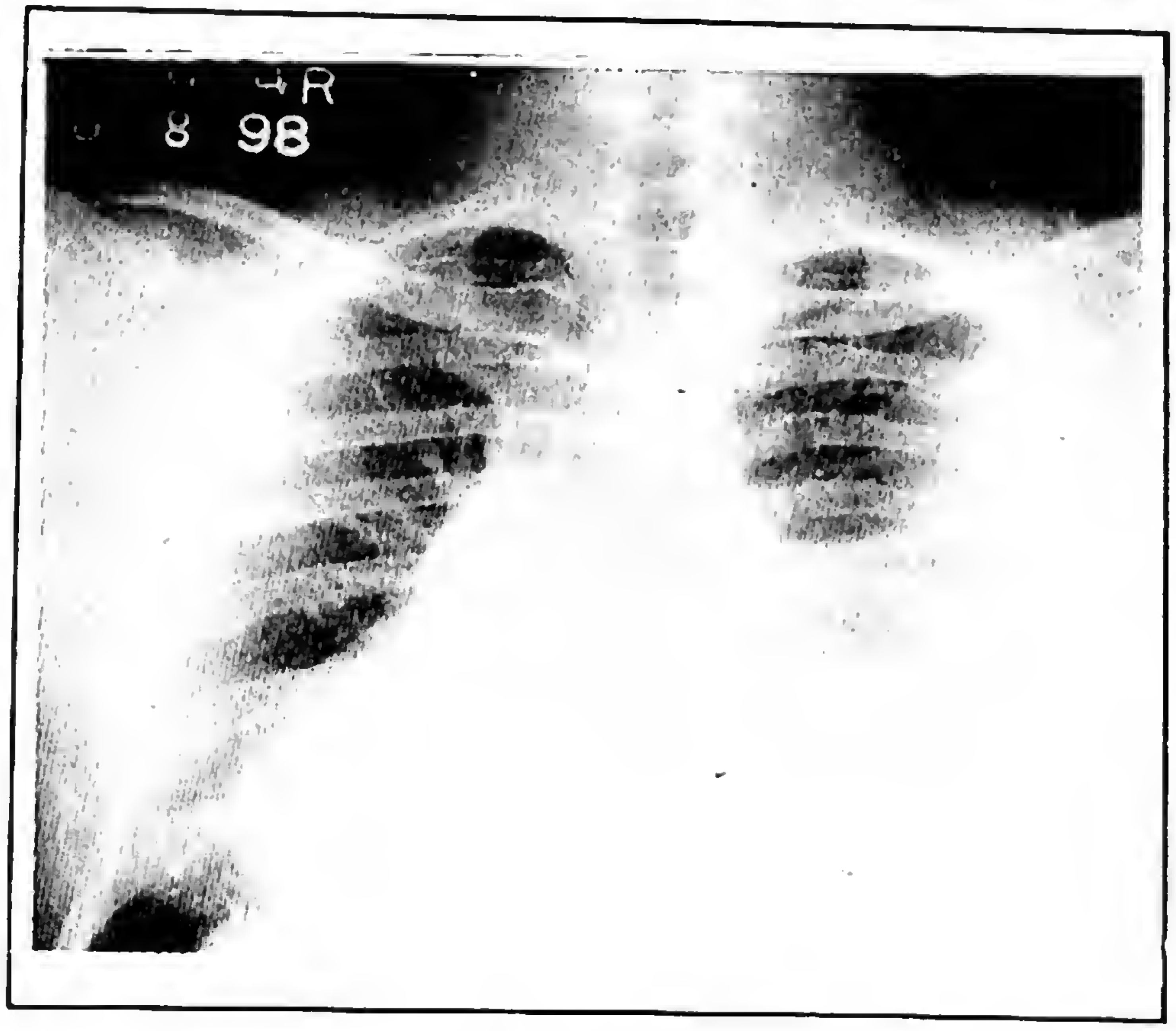

Fig. II

Discussion:

Injuries to the diaphragm may be followed more commonly by immediate or rarely by delayed herniation of abdominal viscera into the chest. Traumatic diaphrgmatic herniation is uncommon on the right side as the cushioning effect of the liver protects the right leaf of the diaphragm[1]. In this patient, the defect was on the left side of the diaphragm.

There is discomfort immediately after the herniation of the viscera in the chest. However, patients get accustomed to the discomfort if herniation does not increase rapidly with passage of time The adaptation to the herniation is sometimes so much that some patients even forget the history of traumatic injury[2].

This case presented with complaints of dyspnoea which increased on exertion. Physical signs may be related to the chest or the abdomen and vary according to the organ herniated into the chest or to whether the presentation is immediate or delayed[3]. Immobility of the left chest, tympany, diminshed air entry and bowel sounds in the chest with displacement of the heart to the right are classical signs which may be associated with the diagnosis.

The diagnosis was made on the clinical suspicion and radiological investigations: The availability of C.T. Scan which has simplified, the diagnosis in this case showed bowel loops in the left pleural cavity. Drews et al[4] has recommended barium rentgenography in all cases of thoracoabdominal trauma.

The size of the defect in the present case was 6 cms x 6cms. Bryer et al[1] reported that the size of the defect depends on the types of trauma and it is larger in blunt trauma. This is true in this case.

Operative repair was through a left posterolateral thoracotomy through 6th intercostal space. Additional laprotomy approach was required because of difficulty in reducing the hernia. Elbert et al[3] has reported that transthoracic approach is satisfactory in early and late repairs. A combined approach has been recommended by Hegarty et al[5].

A prolene mesh was used as a prosthesis to bridge the defect as it was difficult to close the defect by primary suturing. Elbert et al[3] and Desforges et al[2] have recommended the use of prosthesis in their series.

But postoperatively reactionary pleural fluid was seen in this patient. Increased pleural reaction seen reported by Elbert et al (3). this probably due to the inflammatory reaction to the foreign material used to close the defect. The pleural fluid also could have come from abdominal cavity through the mesh.

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ASCARIS LUMBRICOIDES IN THE EYE - A FAMILIAR PARASITE IN AN UNUSUAL SITUATION

A.R. Nasti M.S.; Abdul Gani Reshi M.S.; Parvaiz A. Handoo M.S.

Abstract: *Ascariasis is caused by a roundworm - ascaris lumbricoides. It is the largest human nematode and effect approximately one-quarter of the worlds population; being specially prevalent in the tropics such as India, China and South East Asia.*

'Kaplan' et al first described an authentic case of an intact young adult ascaris extracted from the nasolacrimal duct of an 18 month old African girl from Durban, South Africa[1]*. A similar case was reported by Roche, who found an ascaris in the nasolacrimal duct*[2]*. Another case was reported by M. Balasubramaniam who extracted a live female, immature ascaris worm from the lacrimal passage*[3]*.*

We report an additional case of live ascaris lumbricoides extracted from left lacrimal punctum of a 15 year old girl.

Key words: *Occular Ascariasis, Nasolacrimal duct*

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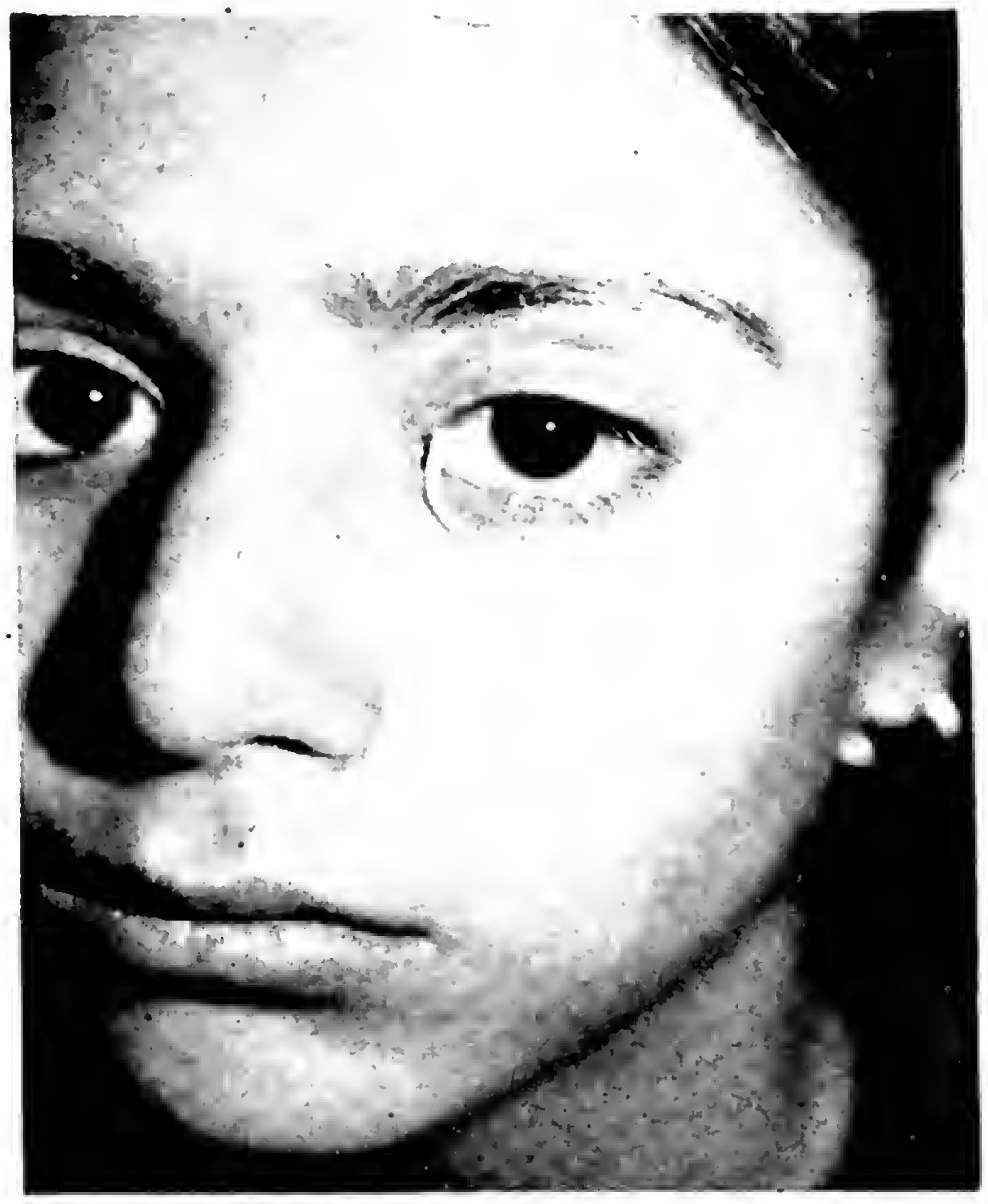
Case Report:

A 15th old girl presented to our outpatient department with something white, thread-like, coming out from the inner canthus of left eye since one day.



On examination, a small white threat - like material whose one end was lying in upper part of left side of face and the other end was invisible, was found coming out from the upper punctum of the left eye. On close examination, it appeared to be a small nematode (Ascaris lumbricodes) showing minimal movements on touch. Under topical anaesthesia the worm was pulled out with the forceps. It was found to be a white live round worm 61/2 long and 1mm thick. The worm was identified by Pathology department of Medical College Srinagar, and was confirmed to be a female ascaris lumbricoides.

The visual acuity was normal in both eyes. There was no allergic manifestation either in the conjuctiva or in general. Slit lamp examination of the eye was normal. The right nasolacrimal passage was free.

Stool examination for ova and cyst of ascaris was positive. Total and differential count showed no eosinophilia. The patient did not return for follow up examination.

Discussion:

Ascaris lumbricoides is the largest intestinal nematode parasitising man. Man is the only definitive host of ascaris lumbricoides. This parasite is unique in that it passes its entire life cycle in one host. Continuance of the species is ensured by transference from one host to another. The female is capable of laying both fertilized and unfertilized eggs. The mother female worm has an enormous egg laying capacity liberating about 200,000 eggs, daily. The eggs of ascaris behave like an inert material. The larva produces an irritant fluid due to the presence of ascarase, resulting in allergic manifestation. The body fluid of ascaris lumbricoides, when absorbed, is toxic and may damage the tissues.

The worm in the eye is known to cause sub-conjuctival mass, granulomatous iridocyclitis, choroiditis (macular or paramacular) recurrent vitreous hamorrhage, periphelebitis, papilloedema, chronic dacryocystitis and invasion into the subretinal space.[1]

Ascaris larva do not normally develop in the eye as is shown by animal experiments with the intraocular

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injection of ascaris ova. In this girl, the possible way the worm could have reached the eye is by migration of larva into the lung alveoli, thence to the bronchi, trachea, nasopharynx and ultimately getting regurgitated into the nasolacrimal duct and then migrating out into the conjuctival sac through the lacrimal punctum.

Management of ascariasis includes treatment with either mebendazole (100mg twice a day for 3 days) or Pyrantel Pamoate (11mg/kg/ in single dose). For ectopic infections without systemic involvement, surgical removal is the only therapy recommended in the literature.

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OBITUARY

I am writing with profound grief for a man whom I held in high esteem and kept very dear:- **Dr.Nissar Hussain Jan**,passed away at the age of 45 on 10.07.2000, after fighting a prolonged illness. This he did with tremendous courage and patience without disturbing his work schedule.

He graduated from Srinagar Medical College in 1977 and was transferred to Bone & Joint Surgery Hospital, Srinagar in 1991 as an Assistant Surgeon.

He played a pivotal role in the management of mass causalities in the last decade of turmoil in the valley. Love for his job and concern for people kept him on tender hooks thus approachable and available to Hospital staff and patients even at odd times and that too at peak of his illness. He was working two days before he actually succumbed to illness.He leaves behind pleasant memories which I shall always cherish. Haji Sahib will be remembered by this hospital for a long time.

May Allah shower him with mercy and blessings.
Aamin

Prof.Ghulam Rasool Mir
Bone & Joint Hospital,
Burzulla ,Srinagar.

MULTISYSTEM ORGAN FAILURE (MSOF) IN ALUMINIUM PHOSPHIDE (ALP) POSIONING

Vijay Gupta M.D.; Jaipal Singh M.D.; S.S.Doodan M.D.; S.K. Bali M.D.

***Abstract:** The widespread changes at celluler trend encountered in ALP poisoning has a potential to involve not only the heart and lungs but also the liver, Gi tract, kidneys etc., if the patient survives long enough. These extended manifestations are rarely seen as death occurs within 24 hours in most cases due to cardio vascular collapse or acute hypoxic respiratory failure in both. We present a case of multi system organ failure due to ALP poisoning who survived and in whom the cardiac involvement developed, not early which is usual, but very late.*

***Key Words:** aluminium phosphide, Poisoning, multi system organ failure.*

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Case Report

A twenty years old unmarried female was brought to us 2½ hours 30 mts. after consuming one tablespoon (3.0 gm.) of quickphos (ALP). The patient had vomited on her way to the hospital. Examination revealed a drowsy female with cold and clammy extremities, complaining of pain in epigastrium and nausea. Her pulse was feeble and B.P. was unrecordable. Respiratory rate was 20/mt. and pupils were normal and reacting to light, she also had tenderness over abdomen. Investigations at admission revealed:-

A normal haemogram and urine analysis, Serum Chemistry was also normal (urea, creatinine, sodium and potassium), so too was skiagram of chest, however ECG showed sinus tachycardia and there were no ectopics.

She was managed with-gastric lavage, intravenous dopamine, fluids, oral anacids, intravenous H2 blockers and antibiotics.

The patients condition remained unchanged the next day, however B.P. came upto 90/60mmHg but on third day she deteriorated once again going into shock, her urine output declined and S. urea and S. creatinine rose to 208.and 6.3 respectively. The patient was once again managed with dopamine infusion and other necessary measures and though the B.P. rose to 112/84, she still remained oliguric (urine output 100 ml in 24 hrs.) hence she was put on haemodialysis. Despite the above measures the patient continued to deteriorate as she had an episode of haematemesis (B.T., C.T & platelets were normal), she became febrile, dyspnoeic with bilateral basal crepitations and persistent oliguria. Patient was given blood transfusion, another (heparin free) haemodialysis and switched over to parentral ceftriaxone and metronidazole, rest of the management continued as befroe thereafter the patient started showing improvement, her urine output increased to 600 ml and continued to increase over the following days, her B.P. stabilized, fever started decreasing and there was no further episode of UGI bleed. However interestingly her daily serial ECG's which in anterolateral leads had earlier revealed tachycardia only, showed ST depression on the 12th day of admission and hence trimetazidine was added. The patient continued to improve thereafter both clinically and parameter wise and was finally discharged on the 28th day of hospitalization.

Discussion;

The patient's diagnosis of ALP poisoning was based on:

i) Definite History.
ii) Presentation of container by father.
iii) Characteristic clinical picture.

The toxic effects of ALP are due to phosphine ($PH3$) gas which gets liberated once it makes contact with water or acid in the stomach, however instances of fatal exposure to inhaled phosphine gas have also been reported[1,2], the gas acts by inhibition of electron transport resulting in preferential inhibition of cytochrome oxidase in a non-competitive manner[3]. It is also postulated that phosphine produces primary hypoxia of the tissues and experimentally there is evidence of generation of free radicals. In addition there is extra mitochondrial release of hydrogen peroxide[4], accelerated lipid peroxidation and transient hypomagnaesemia and hypomagnocytia[5]. These changes can result in widespread mainfestations, involving the heart, lungs, liver, G.I. Tract, Kidneys and adrenals etc., out of which G.I. Tract, heart and lung mainifestations

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are immediate whereas liver and renal manifestations are late and uncommon[6]. Since majority of patients die either due to cardiovascular collapse or acute hypoxic respiratory failure or both, within 24 hours multisystem organ failure (MSOF) is rarely encountered[6] and nearly always fatal. However the present case was not only a case of MSOF, but also survived. What was even more interesting was the very late onset of cardiac involvement, possibly because of prologned slow release of phosphine as has been demonstrated in experimental studies and clinically by chugh et al[7], and this has been blamed for extended toxicity. Cardiovascular effects and ECG changes in ALP poisoning may be due to direct toxic effects of the poison on myocardium, cellular anoxia due to inhibition of mitochondrial cytochrome-C oxidase enzyme, disturbances of ionic permeability and transmembrane action potentials of cardiac cells and associated acidosis and hypomagnesemia. Nevertheless, prolongation to such an extent as in the present case has to the best of our knowledge not been reported in the literature so far.

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EFFICACY OF A HERBAL FORMULATION 'OPTILIV' AGAINST HAPATOTOXICITY OF ANTITUBERCULOSIS DRUGS : A DOUBLE BLIND STUDY

Vijay K. Singh MBBS, Ph.D.

Abstract: *Hepatitis can be caused by all anti-tuberculosis drugs though it is very rarely due to ethambutol or cycloserine. The three most important first line anti-TB drugs viz, Isoniazid, Rifampicin and Pyrazinamide are all hepatotoxic. The beneficial effects of a herbal preparation "Optiliv" against hepatotoxicity induced by there drugs presented in this paper.*

Key words: *Anti tuberculer drugs, Hepatitis, Herbs, Optiliv.*

JK-Practitioner 2000; 7(4):

Introduction

The frequency of hepatitis as an adverse effect of anti-tuberculosis chemotherapy is low, analysis of large studies all over the world suggesting a frequency of 0 to 5 percent. In Indian studies, however, the incidence of clinical jaundice with short course chemotherapy using these 3 drugs is variable, ranging from 2.5%[1] to 22%[2]. The wide variation may be due to poor nutrition and subclinical infective hepatitis or chronic liver diseases in this population.

Hepatotoxicity induced by antituberculosis drugs leads to non-compliance of drug therapy leading to default, drop-out and ultimately poor success rate. It was, therefore, decided to use a herbal formulation 'OptiLiv' known to be hepatoprotective in experimental studies.

Optiliv has been reported to be safe and has no toxicity following long term administration in rats[3].

Hepatoprotective action of this formulation has been reported in both in vitro and in vivo experimental models. Clinical trials on normal healthy volunteers (Phase-I) have established the safety and tolerability of OptiLiv[4,5,6].

Herbal ingredients in OptiLiv are claimed to be very useful in treatment of liver disorders and many of these have been used individually or in combination for their hepatogenic and hepatoprotective and anti-oxidant actions[7,8,9].

Materials and Methods

The design of this study was randomised, placebo controlled, double blind trial. Drug code was provided in a sealed envelope which was kept secret till final analysis of trial was over.

Patient Selection

62 newly diagnosed sputum positive patients of tuberculosis were included in the study. In addition to these 62 cases, 8 patients of confirmed tuberculosis were further added who were already on anti-tuberculosis drugs and were referred to our OPD for drug induced jaundice.

All the 62 newly diagnosed cases received 2 months intensive phase of Ethambutol (E), Isoniazid (H), Rifampicin (R) and Pyrazinamide (z) followed by continuation phase of isoniazid (H) and rifampicin (R) for a duration of 4 months. The referred 8 cases of drug induced jaundice were all in 2 months intensive phase of treatment with RHEZ. All the patients included for trial were investigated for routine blood, urine and liver function tests on day 0, 7, 14, 30 and 45.

Drug Administration

A total of 70 patients (62+8) were randomised for the trial. 62 newly diagnosed cases received RHEZ but 8 referred cases did not reveive any anti-tuberculosis medication. Of the 70 total cases, 36 (32RHEZ + 4) were assigned to group A to receive the drug labelled "A" (containing OptiLiv) and 34 patients (30RHEZ + 4) were included in group "B" to receive the drug labelled "B" (containing placebo). Randomization was done with the help of 'random number table'. Nine patients (7REHEZ + 2) in group A and 4 (all RHEZ) in group B could not be followed after initial evaluation, so their data were not included in the final analysis.

Both drugs A and B were dispensed in capsule form of the same colour, size and shape. Informed consent was obtained from each patient, or his/her relatives, before inclusion into the trial. Each patient under treatment in group A was given 1 capsule of OptiLiv twice a day for at least 8 weeks (during the intensive 2 months phase of

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RHEZ). Each patient in placebo group was given placebo capsules, according to the same schedule.

The composition of OptiLiv is mentioned below:
Each 450 mg Capsule contains extracts of

Andrographis paniculata	75 mg.
Picrorhiza kurroa	75 mg
Eclipta alba	75 mg
Boerhaavia diffusa	45 mg
Azadirachta indica	30 mg
Swertia chirata	3 mg
Solanum nigrum	37.5 mg
Terminalia arjuna	15 mg
Aphanamixis rohituka	15 mg
Terminalia chebula	30 mg
Furmaria indica	22.5 mg
Excipients	q.s.

Results and Discussion

Both the groups were matched in most of the demographic and other characteristics to eliminate the possibility of any biased conclusion. Poor nutrition, alcoholism, chronic active hepatitis for example, might increase the RHEZ toxicity and may probably after the effect of OptiLiv, hence such cases were excluded from the study.

Table-1 Effect on Appetite, with and without Optiliv

Parameter	Group A (Optiliv)	Group B (PLacebo)
Total No. of patients	27(25+2)	30(26+4)
Appetite improved in	18	4
Appetite did not change in	8	7
Appetite decreased in	1	19

None of the patients experienced any side effect. In group A, the remarkable response was, markedly increaed appetite as compared to group B, as shown in Table 1.

The marked improvement in appetite by OptiLiv is worth considering in detail. All the 18 patients in whom OptiLiv increased the appetite, also had marked feeling of well being, their bowel movements became regular and stools were well formed. Either OptiLiv normalised or enhances persistalsis leading to a regular bowel movement and hence resulting in a feeling of well being or on the other hand, the first effect may have been central and therefore resulting in a automatic improvement in gut movement.

Alternatively the basic effect of OptiLiv might have been rather the turning of the biological clock. Circadian variations on the effect of drugs are now well known to enhance the efficacy of Theophyllines in bronchial asthma. The biological rhythms have been stressed by Ayurveda as "Dinacharya". The ancient Ayurvedic physicians believed that "Dinacharya" reinforces the biological rhythms and many herbal formulations help to restore the disturbed rhythms. OptiLiv not only enhanced the appetite but also normalised the appetite — satiating rhythms. The patients on OptiLiv (Group A) not only received and consumed food in time but also felt satisfaction after the food. This was altogther absent in Group B patients. The use of ATT per se can increase the appetite and feeling of well being. However both the groups A&B had been on ATT but group A had clearly far better appetite than group B.

Table-2: Liver Function tests and Hb during RHEZ Treatment, with and without Optiliv

Number of Patients (n) Group A=25 (on Optiliv Treatment) | Group B = 26 (All RHEZ (Control)

Parameters	Day-0 Group A	Day-0 Group B	Day-7 Group A	Day-7 Group B	Day-14 Group A	Day-14 Group B	Day-30 Group A	Day-30 Group B	Day-45 Group A	Day-45 Group B
Biochemical S. Billirubin mg% Total	0.56 ± 0.08	0.50 ± 0.06	0.60 ± 0.06	0.64 ± 0.10	0.58 ± 0.08	0.68 ± 0.10	0.50 ± 0.06	0.76 ± 0.10	0.54 ± 0.06	0.74. ± 0.08
SGOT I.U/L	9 ±1.38	11.74 ±1.24	17.84 ±1.74	24.26 ±1.78	16.34 ±1.66	28.32 ±1.08	15.08 ±0.99	26.00 ±1.12	12.00 ±0.80	25.00 ±0.72
SGPT I.U/L	16 ±1.76	18.00 ±2.08	18.90 ±1.03	26 ±1.75	17 ±1.78	33 ±1.03	19 ±1.00	36 ±1.06	22.8 ±1.90	34 ±2.08
Alkaline Phosphatase I.U/L	44.75 ± 6.08	47 ± 5,86	76 ± 3.88	52 ± 5.16	78 ± 6.90	98 ± 7.08	86 ± 5.45	111 ± 6.80	92 ± 7.86	118 ± 6.86
Haemato-logical Hb gm%	10.24 ± 1.32	9.75 ± 0.3	10.24 ± 1.32	9.60 ± 0.26	13.66 ± 0.36	9.00 ± 0.18	14.33 ± 0.32	9.50 ± 0.28	14.20 ± 0.22	10 ± 0.24
Weight (in Kg)	42.33 ±5.86	41.75 ±6.33							48 ±4.32	44.22 ±2.08

Patients on OptiLiv (Group A therefore gained much better weight than those of the control group (Group B).

Hepatitis induced by Antituberculosis drugs often occurs within 45 days[10] of drug administration and may be related to the period of maximum induction of the hepatic microsomal enzyme system by Rifampicin which starts to peak after 10 days[11]. Even though the course of this hepatitis is usually benign it may necessitate drug withdrawl once jaundice becomes overt[12].

The clinical and biochemical features of ATT induced Hepatitis are indistinguishable from those of viral hepatitis and no diagnostic markers exist. In any case the reported incidence of hepatotoxic reactions during ATT therapy is higher in developing countries and related to the endemicity of viral hepatitis. The present study indicates that OptiLiv affords definite protection against ATT induced hepatitis. This is evident from the early recovery in liver function tests. The feeling of well being induced by Optiliv could be due to an increase in appetite by it and consequent weight gain on one hand and on the other had better assimilation of food by the use of Optiliv can not be ruled out. This factor could be a boon for improving compliance of antituberculosis drugs in patients who resent the necessary long term course of these drugs.

The mechanism for increase in appetite can not be pin pointed by this study but weight gain and increased appetite has been well documented in experimental animals and in Phase-I clinical trials in humans when given Optiliv. Other clinical studies have also substantiated this kind of effect[7].

Table-3: Liver Function tests and Hb in ATT induced Jaundice, with and without Optiliv

Number of Patients (n) with ATT induced jaundice without RHEZ	Group A = 2	(On Optiliv Treatment)
	Group B = 4	(control)

Parameters	Day-0 Group		Day-7 Group		Day-14 Group		Day-30 Group		Day-45 Group	
	A	B	A	B	A	B	A	B	A	B
Biochemical S. Bilirubin mg% Total	4.58 ± 0.24	3.85 ± 0.46	3.86 ± 0.22	3.05 ± 0.08	2.55 ± 0.46	2.78 ± 0.04	1.65 ± 0.23	2.00 ± 0.46	0.64 ± 0.08	1.55 ± 0.10
SGOT I.U/L	102 ±1.46	118 ±1.78	92.4 ±1.78	116 ±1.24	72.60 ±0.80	95.5 ±1.34	40.5 ±0.06	60 ±1.28	17.74 ±1.40	32.06 ±0.88
SGPT I.U/L	48 ±0.24	42.5 ±1.75	40 ±1.12	40 ±1.6	32.5 ±1.06	36.88 ±1.24	24.6 ±1.9	32.40 ±1.06	18.92 ±1.04	30 ±0.08
Alkaline Phosphatase I.U/L	326 ± 8.05	388 ± 7,86	240 ± 8.80	202 ± 6.56.	186.5 ± 7.65	194.5 ± 6.04	105 ± 3.88	152.6 ± 4.78	92.5 ± 6.80	140 ± 7.80
Haemato-logical Hb gm%	10 ± 1.32	8.5 ± 1.46	10.5 ± 1.07	9.00 ± 0.48	11.00 ± 0.08	8.76 ± 1 50	12.75 ± 0.50	9.5 ± 0.60	14.5 ± 0.05	10.75 ± 0.06

OptiLiv contains standardized extracts of constituent herbs rather than crude powder or mass extracts, which could ensure higher bioavailability of active constituents, for quick and sustained action. The dosage convenience with 1 capsule twice daily dosage of OptiLiv as against several tablets, several times a day with other products, helped better patient compliance.

OptiLiv contains the extract of many internationally recognised herbs known for their hepatogenic and hepatoprotective actions such as Eclipta alba, Picrorhiza kurroa, Andrographis paniculata, Boerhaavia diffusa and Aphanamixix rohituka which are absent or used in negligible quantities in other formulations. OptiLiv also contains herbs like Swertia chirata, Solanum nigrum and Azadirachta indica which are known for their digestive, enzymatic and choleretic actions which help to restore normal digestive functions. It appears that the combined action of all the ingredients is responsible for beneficial results observed in this study.

Active constituents of picrorhiza kurros have been reported to provide hepatoprotection and reverse toxiant-induced alterations in the enzymes of plasma membrane, mitochondria, microsomes and changes in gross level of nucleic acids and lipid peroxides[8,9]. They showed protective effects against rifampicin and ethanol induced hepatic dysfunction and enhanced the viability and oxygen uptake of hepatocytes[13]. They stimulated regeneration of hepatocytes and showed protection in hepatic glutathione content, glutathione-S-transferase, aniline hydroxylase, aminopyrine demethylase and cytochrome p450 activity. A promising anti-hepatitis-B virus surface antigen like activity was noted which differed from classical virus neutralization and also inhibited purified hepatitis B virus antigens prepared from healthy carriers[28,29].

Picrorhiza kurroa provided earlier clinical and biochemical recovery in the patients with acute viral hepatitis[11] and also showed significant improvement in symptoms like anorexia, nausea and vomiting[15,16].

The research studies have shown that the active constituents of Andrographis paniculata increased the rate of mitosis of hepatocytes and DNA, RNA and protein synthesis in regenerating liver[26]. They exhibited a strong choleretic action and provided symptomatic relief to the patients with ineffective hepatitis[18,19]. A paniculata is known to accelerate intestinal digestion and absorption[20,21]. Pretreatment with A. paniculata caused induction of microsomal enzymes and activation of brush border membrane-bound hydrolases, lactase, maltase and sucrase in small intestine[22]. The active principle from A. Paniculata-Andrographoloids shows hepatoprotection against Galactosamine induced hepatic injury and isoniazid induced hepatotoxicity. The probable mechanism for this is by blockade of the microsomal enzyme system.

Some researchers observed tha Eclipta alba caused inactivation of hepatitis-B virus surface antigen and restored Na-K-ATPase activity of hepatocytes to normal level during hepatic injury by various hepatotoxic agents. This indicates that E. alba maintains active transport system of hepatocytes even after toxic challenge[23,24].

Boerhaavia diffusa extract significantly enhanced the bile flow and proved beneficial in chronic alcoholic cirrhosis, jaundice, general weakness, anaemia and also in viral hepatitis[25,26,27]. Terminalia chebula has got the property of evacuating the bowel completely. It is useful in chronic constipation, peptic ulcer and as a general tonic[25].

OptiLiv proved effective in treatment and faster recovery from acute viral hepatitis as shown by rapid clinical and biochemical improvements, without any relapse[7].

It is indeed likely and highly probable that the beneficial effects of OptiLiv shown in this study against hepatoxicity of Anti-tuberculosis drugs is not only a sum total effect of its various ingredients, rather the synergistic effect appears to be greater than the relief offered by the use of individual herbs since the mechanism of action of various herbal ingredients of OptiLiv is at different sites and different levels. This makes the hepatoprotective action of each synergetic to that of the other and the resultant effect is greater than what would be observed by a simple additive mechanism. From the study it is clear that OptiLiv not only prevents drug induced hepatitis due to antituberculosis drug but also quickly reverses the liver damage already caused by such therapy since it gave equally good results when used as an adjuvant and hepatoprotective in short course ATT regimen and when used to treat hepatitis caused by previous intensive phase ATT. In addition it produces early subjective improvement in the form of increase in appetite and a feeling of well being.

This study thus brings forth clearly the benefit of adding OptiLiv capsule as an integral part of Intensive phase ATT in order to prevent overt Hepatotoxicity and this minimises the chances of treatment default and or discontinuation, which is a common cause for development of resistance to standard ATT in our country. The administration of OptiLiv also had other beneficial effects such as improvement in appetite alongwith reinforcement of biological rhythms including normalisation of appetite-satiating rhythms providing satisfaction after the food. Further OptiLiv also ensured regularity of bowel movement and well formed stools as well as marked improvement in the feeling of well being.

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BLADDER RECONSTRUCTION USING DETUBULARIZED INTESTINAL SEGMENTS — FROM VIEW POINT OF MATHEMATICS

Bladder reconstruction is being currently done by using intestinal segments wether from small bowel or large bowel depending on circumstances and surgeon's choice but aim in all surgeries is to have a complaint neo-bladder i.e., a bladder with sufficient capacity so that frequent micturation is not troublesome and pressure inside bladder does not go above ureteral pressures. Besides we try to construct new bladder using minimum segment of intestine so that incidence of diarrhea and nutrient deficiency is lesser. In this perspective usage of opened segments of bowel provide better results than tubular ones.

To support above we have to try to go into mathematical considerations. When a bowel segment is used in its original tubular form, its volume $(v)=nr^2x1$

r = radius of segment
l = length of segment

So if the segment we have taken is of ileum with approximate radius of 1 cm and length of segment taken is 10 cms, its volume when taken in tubular form will be nr^2 x 1=25cc and now if we open the bowel and create a patch or pouch, the volume will increase as now geomatrically structure of sphere has been created instead of cylinder and volume of sphere is $4/3\ nR^3$ which is 47 cc in this case. So volume gain in this case is 47-25=22 cc i.e., 86% in this case[1].

Applying same formula we can compare a few more examples (Table 1).

Application of above mentioned facts can enable us to calculate augmentation volume of small bladders which have been reonstructed using bowel segments, this can guide one to calculate how much of bowel segment must be used to form a new bladder with a specified capacity (Table 2).

Detubularized segments have an additional advantage of having better accommodation[2] as compared to tubularized segments because as per Laplace's lae $T=pxr$

T = Mural tension or stretch resistance
p = intravesical pressure
r = radius of cylinder

In normal functioning as 'r' increases due to bladder filling, tension in bladder wall increases to keep 'p' constant[3,4]. So when 'r' is less as in tubularized segments, wall tension will be significantly high at the same pressure when compared to detubularized segment with higher value of 'r', hence accommodation is more in detubularized segments as compared to tubularized ones.

Besides the above parameters detubularized bowel segments have been shown to have better compliance. Compliance 'C' is given by AV/AP where AV is volume increment and AP is pressure change seen with this volume increment. Viscous structures oppose the rate of stretch and delay recovery so a viscoelastic structure under tension during filling will elongate with time and return less readily to its original configuration[5,6]. Since bowel wall is viscoelastic so at a constant pressure patches and pouches created during augmentation of bladder will show more compliance as their radius is more (Laplace's law).

Comments

After analysis of above mentioned mathematical variables and their importance regarding reconstruction of bladder it is absolutely clear that detubularized bowel segments are far better as compared to tubularized segments.

Table 1

Change in volume in same segment of intestine when it was detubularized.

Length (cm) of intestinal segment	Radius (cm) of intestinal segment	Cylinder Vol. (cc)	Sphere Vol. (cc)	Gain(cc)	Gain (%)
10	1	25	47	22	86
10	1.5	57	86	29	52
10	2	101	132	32	32
10	2.5	157	185	28	18

Table 2:

Capacity of new bladder after reconstruction with bowel segments of varied lengths.

Bowel length used (cm)	Diameter of bowel (cm)	Original volume (cm)	Augumentation volume (ml.)
10	4	50	250
20	2	50	250
20	4	50	532
50	2	50	697
10	2	100	203
20	2	100	327
20	4	100	630
50	2	100	840
10	2	150	380
20	2	150	530
20	4	150	875

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OUTPUT CONSISTENCY OF C-60 (THERATRON-780) 15 YEARS REPORT

Sher-i-Kashmir Institute of Medical Sciences commissioned Department of Radiotherapy in 1982. The Radiation Standards and Dosimetry Laboratory in the Department of Medical Physics and Bioengineering of this Institute was also established in the same year. This lab was equipped with high quality dosimetry equipment, quality assurance kits, Radiation field analyzer, Phantoms and other geometrical tools. The staff and Faculty working in this laboratory was trained at the Division of Radiological Protection (D.R.P.) , BARC, Bombay, various leading Radiotherapy centres of the country and abroad. One of the objectives of this laboratory is to review dosimetry and to ensure high quality radiological physics services once a decision is made to utilize radiation for the treatment of cancer patients. The laboratory also provides continuing education and technology transfer for the medical community in fields related to radiation and cancer control.

Table 1

Dose Output of CO-60 for 10x10cm at SSD-80cms

Year	Av. Actual Output Gy/min.	Av. Using decay factor Gy/min.
1981	2.6623	2.6076
1985	2.3402	2.3174
1986	2.3028	2.2930
1987	1.7664	1.7523
1988	1.5690	1.5747
1989	1.4101	1.3967
1990	1.2554	1.2483
1991	1.1234	1.1148
1992	0.9774	1.0002
1993	0.8575	0.8703
1994	0.7518	0.7519
1995	0.6531	0.6506
1996*	2.6122	2.5681
1997	2.3310	2.3375

**Installation of New Source*

In addition, the laboratory participates in International Atomic Energy Agency(IAEA)/World Health Organization(WHO)/Thermoluminiscence Dosimetry (TLD) inter-comparison programs to ensure dosimetric correctness and consistency for intra-institutional clinical trials and also shifting of patients from one center to another center for treatment.

The cobalt-60 source was loaded in the machine (Theratron-780) in February, 1984. The activity in March, 1983 was 10731 curies. The output on first dosimetry procedure in February 1984 was 2.75Gy/min for 10x10 cms fields size. The output was measured using 0.6cc chambers (2571/2581) with Ionex/Farmer. The principal goal of the Radiation Standard and Dosimetry laboratory is to ensure by review that the output of the Unit is within + 3% of the stated and that the treatment dose calculation methods are within 5%. The methodology used consists of[1] Calibrating one secondary Standard Dosimeter with the national standard at BARC, (2) Using this dosimeter as a standard for the Institute, (3) calibrating the field dosimeters with the Institute standard, (4) Using temperature and pressure as communicated by meteriology department and applying the corrections with the ones measured at the laboratory, (5) Calibrating the field dosimeters with the reference source, (6) Conducting the output measurements every month alongwith other checks on machine Cobalt-60 (Theratron-780).

Table II

Consistency check of dosimeters for Output Measurement of Co-60

Dosemeter	Values obtained	Permissible
Ionex-2500/3	+ 0.125% to + 1.89%	+2%
SSD – 058	+ 0.018% to + 1.73%	+2%
SSD – 072	+ 0.12% to + 0.97%	+2%
Farmer – 2570	+ 0.76% to + 0.79%	+1%

Every month during 15 years the output was directly measured and compared with output using decay factor by usual methods. The laboratory has established and maintained radiation measurements dose calculation standard through periodic review meetings. The intercomparison of the dosimetry has been made whenever approached by Radiation standards laboratory of BARC and the results have been found within the limits as provided by International Atomic Energy Agency(IAEA)/World Health Organization(WHO) intercomparison programme. This has always remained within + 5% except once when there was some problem with the Theratron Unit.

The source was again loaded in February 1996 with a source strength of 10684 curies. The first radiation output was 2.68Gy/min for 10x10cms field. The percentage error has always been below 1% excepting in some cases when it was in the range of 1.84-2.7% respectively.

The department entered into nation-wide intercomparison programme conducted by BARC in collaboration with WHO. The results in this case were also within 1% as compared to dose output using decay corrections.

We have been calibrating our dosimeters every 3 years with national standards and our dosimeters are calibrated with the one calibrated at BARC using inter-comparison phantom. Output has been found to be accurate within 2% for the last 15 years.

The output measured by the standard techniques[2] and from theoretical value using decay factor are shown in table 1. The output of the machine at the time of commissioning viz first source loading in February 1984 was 2.7524 Gy/min. The output at next dosimetry was 2.7034 Gy/min. On the 2nd. Source loading in February 1996 and after the next dosimetry the output was 2.6838 Gy/min. and 2.6517Gy/min. respectively the calculated value using decay corrections was 2.6543 Gy/min. for a field of 10x10cms. The discrepancy in the in the measured and calculated outputs for the 15 years varied between 0.10% and –1.96%. This variation has been always within +2%, a result which is consistent with the prescribed protocols[3,4,5]. The consistency of various dosimeters used for output measurement of Cobalt-60 using Sr-90 check source is shown in table II. It is seen that the variation has never been more than 2%.

The result of TLD/WHO postal inter-comparison programmelie between –1.7% and 3.5% which is within the normal limits. However, a value for the year 1998, is not within the permisible range which is due to the problem in the machine. This was rectified. The later results confirmed this. The results indicate a trend towards achieving uniformity in dosimetry procedures. The review process has been effective in identifying the deficiency and effecting the corrections.

It is suggested that all the Medical physics departments should have at-least 3 secondary standard dosimeters with check source. The department should calibrate the dosimeter with the primary standard as and when required and it should be kept as a standard dosimeter for the Institute.

The laboratory should participate in the TLD postal dose inter-comparison program. The physics and dosimetry equipment should be procured alongwith the teletherapy unit.

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COLON TRAUMA - CHANGES IN CONCEPTS OF MANAGEMENT

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The first reference to colon injuries can be found in Book of Judges[1], where it is mentioned that.

"Ethud put forth his left hand, and took the sword from his right thigh, and thrust it into his belly. And the hilt also went in after the blade, and fat closed upon the blade, for he draw not the sword and of his belly; and the dirt came out".

Hippocrates regarded all the such wound as deadly, and even Celsus advised that their cure be left nature.[2]

The proper treatment of traumatically injured colon has been the subject of considerable controversy for the past 50 years. Prior to the antibiotic era especially with experience gained from World War I, a conservative approach to the management of such trauma was recommended. This usually consisted of exteriorization of the affected bowel followed by a delayed resection and anastomosis, although a number of surgeons elected to perform primary repair.

In 1943 the Surgeon General of United States[3] issued an order stating that all colon injuries sustained in battle would be treated by performing a colostomy. Based upon this philosophy, mortality rate fell to 30% during World War II. Ogilvie[4] reported significant reduction in mortality attributed to the performance of colostomies in the treatment of colon injuries. He mentions that "the exteriorization of colon injuries, a step which I have repeatedly advocated since the outbreak of war is perhaps the greatest single factor in the improved results, we are able to record". However, in the recent years, there has been a tendency for the surgeon to attempt primary repair in the management of colon trauma. Beall et al[5] managed 80% of 328 colon trauma patients by primary repair with mortality rate of 12.8%. This was the first biggest series favouring primary repair of colon injuries in selected individuals. Edwardokies[6] studied the usefulness of exteriorized colonic repair. By using this technique, the need of formal colostomy has been prevented in 49% of patients who otherwise would have required colostomy. Stone and Fabian[7] conducted randomized non-blinded prospective study and concluded that primary repair should become the method of choice in managing civilian colonic trauma. Same types of results were formed by Adkins[8] Cook[9], Nallathambi[10], Demetriades[12] and Sasaki[13].

In 1996 Pezim et al[14] Surveyed 317 members of Canadian Association of General Surgeons to evaluate their attitude towards use of primary colonic repair in trauma. From this survey they concluded that primary report of colon trauma has definitely established a foot hold in all levels of Canadian General Surgery practice.

Edwards and Galbraith[15] published a leading article entitled, "colostomy in conflict: military colon surgery" and they discussed safety of colonic repair in civilian practice. They concluded that if the results of ongoing research about safety of primary repair are favourable, military surgical doctrine may have to change, since not even military surgeons will be able to justify the obsolete and discredited practice of colostomy. It is now obvious that with the passage of time management of colon trauma has changed from obligatory colostomy to a primary repair.

We have also conducted a study on 70 patients of colon trauma at Sher-i-Kashmir Institute of Medical Sciences[16] and found that primary repair of colon injury was safe in carefully selected cases.

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HOW TO DO CONSCIOUS SEDATION

Naira Sultan Khuroo M.B.B.S.

Defintion

Conscious sedation is a medically controlled state of depressed level of consciousness in which the patient maintains protective reflexes, independently maintains a patent airway, and responds appropriately to verbal and physical stimuli. Conscious sedation is performed by practitioners who are not specialists in anesthesiology. Conscious sedation differs from general anesthesia and the differences are shown in Table I.

Indications

Conscious sedation is indicated for performing procedures in a variety of settings such as emergency room, day care centre, endosdopy laboratories, radiodiagnosis department and cardiac catheterization laboratory.

Procedures include:
- Drainage of abscesses
- Dressing of painful wounds/burns
- Reduction of fractures
- Gastrointestinal and Urologic GI endoscopies
- Cardiac catheterization
- Radiology Department, used in children in controlling movement during computed tomographic and magnetic resonance scans.

Contraindications

Absolute

1. Lack of personnel experienced in airway management or advanced life support, or unfamiliarly with medications being administered for sedation and analgesia.
2. Lack of appropriate monitoring equipment or inability to monitor the patient during the procedure and recovery period.
3. Allergy and sensitivity to relevant medications.

Relative

1 Infants < 3 mo of age
2 Premature infants < 60 weeks post conceptual age
3 History of apnea or disordered control of breathing
4 Cardiorespiratory disease.
5 Hemodynamic or neurological instability
6 Obtundation
7 Facial, dental or airway abnormalities
8 Renal or hepatic disease
9 Neuromuscular disease

Table I: The differences between conscious sedation and general anesthesia

Conscious sedation	General anesthesia
◆ Is a controlled depressed level of consciousness	Is a state of unconsciousness
◆ Protective reflexes maintained	Protective reflees are progressively lost as stages of anesthesia deepens.
◆ Subject independently maintain airway	Needs assistance to maintain airway
◆ Appropriate response to verbal and physicial stimuli	No response to verbal and physical stimuli
◆ Can be performed by any medical Professional	Performed by a anesthesiologist
◆ Can be used for short procedures in number of places in the hospital	Use limited to operation theatre.

Medical Personnel and their Roles

The minimum member of personnel for any procedure utilizing conscious sedation is two: the proceduralist and the nurse.

The physician is responsible for the following:

- Patient selection and assessment pre-procedure
- Medication ordering and/or administration
- Monitoring efficacy and patient safety
- Patient and family education through informed consent

The nurse is responsible for the following:
- Ensuring necessary emergency equipment is readily available
- Administration of medications per-
- Monitor patients response to medications and any alterations in physiological status
- Recognize adverse effects and intervene as necessary
- Completion of conscious sedatio flowsheet.

The physician is in the defined procedural area the time of administration of conscious sedation medication until procedure completed. The nurse will not engage in any tasks that would compromise continuous patient monitoring Sedation administration and recovery of patient occurs int he procedural area. Following recovery, a nurse must accompany the patient to their inpatient and outpatient area.

Table-2: ASA classification - physical status classification of the American Society of Anesthesiologists

ASA Classification	Medical Description of Patient	Comments
ASA I	No Known systemic disease	May have conscious sedation without other consultation.
ASA II	Mild or well controlled systemic disease	May have conscious sedation without other consultation.
ASA III	Multiple or moderate controlled systemic disease(s)	Consider anesthesia consultation
ASA IV	Poorly controlled systemic disease(s)	Mandatory involvement of Anaesthesiology Department.

Patient Selection and Assessment

The need for any therapeutic, diagnostic or surgical procedure and subsequent use of conscious sedation will remain under the individual physician's direction. There must be a documented evaluation of the patients anaesthetic risk prior to administration of conscious sedation using the ASA (American Society of Anesthesiologists) rating. ASA rating is shown in Table 2.

Table-3: Drugs used in conscious sedation

Drug	Age	Route	Dose	Onset (min)	Duration (min)
A) Sedatives					
1. Diazepam	Children	PO	0.1-0.2 mg/kg	30	360-480
	Adults	PO	2-10 mg	30	360-480
	Adults	IV	2-10 mg	30	360-480
2. Midazolam	Children	PO	0.5-0.75 mg/kg	15	60-90
		IV	0.05-0.1 mg/kg	2	30-60
	Adults	IV	1.0-5.0 mg	2	30-60
3. Chloral hydrate	Children	PO	50-100 mg/kg (max 2 mg)	15-60	360
B) Narcotics					
1. Fentanyl	Children & Adults	IV	1-5 mcg/kg	immdiate	45-60
2. Meperidine (Demerol)	Children	IV	0.5-1 mg/kg	1-5	30-180
	Adults	IV	0.5-1.5 mg/kg	1-5	30-180

Equipment/Supplies

At a minimum, the following equipment must be present, in working order and be immediately accessible where conscious sedation is being administered.

A) Inpatient Room

1) **Airway Management Equipment**
- Oxygen source
- Suction
- Face masks
- Laryngoscope
- Endotracheal tubes

2) Non-invasive blood pressure monitor or manual blood presure cuff & Pulse oximeter.

3) **Drugs**

Drugs for conscious sedation
- Midazolam or Diazepam
- Demerol or Fentanyl

Reversing / Emergency drugs
- Naloxone
- Flumazenil
- Epinephrine
- Atropine
- Hydrocortisone

B) On Nursing Unit
- A cardiac arrest cart with defibrillator

Table-4: Anditotes to medication used in conscious sedation

Drug	Age	Route	Dose	Onset	Duration
Reversal Agents					
Flumazenil	Children/Adult	IV	0.01mg/kg (max 0.2 mg) repeat at one min intervals (max dose of 1 mg)	1-2	20-40
Naloxone	Adults	IV	0.4-2 mg, repeat at every 2 min (max 10mg)	1-2	20-40

Drugs

General Guidelines

a) The physiian performing the procedure is responsible for ordering all administered drugs. Therefore, he/she must be familiar with the pharmacological profile of any drug used (i.e. dose range, actions, side effects, possible complications which the physician must be prepared to treat promptly).

b) Short acting drugs which can be titrated to desired effect and can be readily reversed are recommended: long acting drugs and drug administered per rectum and intramuscularly, where absorption may be variable, are not recommended.

c) Small, incremental doses should be titrated to reach the desired effect or "endpoint". Intravenous titration is the only reliable way to achieve a given endpoint (i.e. sedation only, sedation and analgesia). Drug doses for procedure sedation are based on titration to a desired endpoint, not calculated on a milligram per kilogram basis.

d) Rapid drugn boluses ("IV push") are more likely to cause unexpected deterioration than is gradual drug administration over 1-2 min.

- **Choice of Drugs**

  The choice of drugs for conscious sedation is determined by whether sedation or analgesia only demand patients coperation, Midazolam administered intravenously is the drug of choice. Demerol is the preferred drug when anaelgesia is needed during the procedure. Often Demerol and Midazolam are used together for painful procedures. Antidotes to drugs which must be available are Flumazenil and Naloxone (table 4). These agents should be used to reverse drug-induced respiratory depression, not on prophylactic basis in stable patients, since antagonist used is associated with increased re-sedation risk.

Talbe-5: Aldrete score based on clinical observations. The score is obtained by adding the score in each of the five observations.

S.No.	Observation	Score	Definition
a.	Activity	2-	moves all extremities
		1-	moves 2 extremities
		0-	no conrol
b.	Respiration	2-	deep breath and cough
		1-	dyspnea or splinting
		0-	absent effort
c.	Circulation	2-	BP 20% of pre procedure
		1-	BP 210-50% of procedure
		0-	BP 50% of pre procedure
d.	Consciousness	2-	alert
		1-	responds
		0-	absent response
e.	Colour	2-	normal
		1-	any alteration
		0-	Frank cyanosis

- **Drug Administration**

  1. **Midazolam**
     a) Individualize dosage on basis of age, physical status and concomitant medication. Do not give drug by rapid or single bolus intravenous administration. Titrate the dose to the desired effect (end point).
     b) Dilute the drug to a concentration of < 1 mg/ml.
     c) Start with 1 with of the drug and administer slow IV over one minute. Wait for additional 2 minutes to evaluate the response.
     d) If additiodnal drug is required, administer small increments (0.5 mg) slow IV to the desired end point. Wait 2 minutes for additional small increments.
     e) For maintenance of sedation give 25 percent of the dose required to reach the endpoint at the beginning.
     f) Total of 5 mg (for adults) and 3.5 mg (for patients over 60 years or debilitated or chronically ill patients) is usually not necessary.
     g) Reduce drug dose by 30 percent if concomitant drugs like Demrol is used.
  2. **Demerol**
     a. Individualize dosage.
     b. Use diluted drug to 10 mg per ml.
     c. Administer the drug by slow IV to teh desired effect.
     d. Reduce the dose by 25 percent if concomitant tranquilizers are used.

- **End point**

  Sedation is a continuum with infinite end points. The optimal endpoint for conscious sedation depends upon the procedure to be performed, the amount of pain to be inflicted and patients anxiety and cardiorespiratory reserve. For majority of procedures operator demands anxiolysis (calm patient) and sedation (drowsy patient but with clear mentation). Thus the drug could be titrated to end point of "eyes open with slurred speech".

Monitoring and Documentation

- A conscious sedation flow sheet must be completed by a nurse for all patients receving conscious sedation.
- Monitoring should be at 3 stages -
  1) Baseline assessment
  2) Peri-procedure monitoring and documentation
  3) Post-procedure monitoring and documentation.

Continuous heart rate, BP, pulse oximetry respiratory rate and level of consciousness should be recorded before and after drug administration, q 15 minutes during the procedure until patient is fully awake and at time of discharge.

Discharge Criteria

- **Recovery room discharge criteria:**

  Alderte score (table 5) is determined and documented on admission to recovery room. A score of 8/10 is required before a patient is discharged dfrom the recovery room.
- **Home discharge criteria:**

  Prior to discharge home, all the below mentioned criteria must be met.
  a. Vital signs returned to pre-procedure baseline, inform MD if blood pressure is above or below 20 percent of baseline.

b. awake and responsive to commands
c. able to sit, stand, ambulate without assistance
d. Absence of nausea, vomiting and dizziness
e. responsible adult present as escort
f. discharge instructions give to patient and adults.

References:

1. Committee on Drugs American Association of Pediatrics (1999). Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures. Pediatrics 89, 1110-15.
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I Dr. G.M. Malik hereby declare that the particulars given above, are true to the best of my knowledge and belief.

Sd/-
Dr. G.M. Malik

WORLDWIDE EMERGING ANTIBIOTIC REISTANCE

FAROQUE A. KHAN, M.B., M.A.C.P.*

Antibiotic resistance is taking center stage. ACP-ASIM made antibiotic resistance its college theme for the year 1999-2000; news and medical journal articles point to this increasing problem. With increasing globalization, increased travel, and civil unrest in Africa and Asia, it's becoming increasingly clear that the microbes are finding it easier to move around the globe. In fact, The New York Times editorial of June 18, 2000 was titled "Losing Ground Against Microbes."

The issue is a complex one - underusage of antibiotics in poor countries, and overusage in rich countries both play a role in selecting resistant organisms. The use of antibiotics for growth of livestock and poultry has been clearly shown to lead to the emergence and transmission of organisms from animals to humans, and survival of parasites in chlorinated water, etc., etc. Treatable diseases like malaria, gonorrhea, and tuberculosis in some parts of the world can no longer be treated adequately.

The following is a summary of the issues involved and possible solutions which will need the involvement of everyone – policymakers, consumers, and providers. For a detailed review, I suggest the 700-plus page book "The Coming Plague" by Laurie Garret, publisher Farar, Strauss and Gironx, New York 1994 – in particular, Chapter 13 titled "The Revenge of the Germs." Consider the following:

> *A small bacterium weighs as little as 0.00000000001 gram. A blue whale weighs about 100,000,000 grams. Yet, a bacterium can kill a whale! Microbes, not macrobes, rule the world.*
> *Bernard Dixon, 1994.*

ANTIMICROBIAL RESISTANCE – When is it a problem?

Defined as a problem when it requires clinicians to alter antibiotic therapy substantially by substituting more toxic agents, substituting more expensive agents, or utilizing more complex multi-drug regimens.

IMPACT OF ANTIBIOTIC RESISTANCE

Increased morbidity and mortality – especially problematic before widespread awareness; increased and prolonged hospitalizations; remaining effective antibiotics are used more often, leading to greater selective pressure; use of drugs with greater toxicity; use of more expensive drugs; nursing home placement difficulties; cost of isolating patients in the hospital; overall cost to the US as much as $30 billion/year.

CONTROLLING ANTIBIOTIC RESISTANCE

Surveillance; prudent use of antibiotics; maximize the use of vaccines to minimize the need for antibiotic therapy; improved hospital infection control; eliminate prophylactic use of antibiotics in agriculture; new antibiotics; worldwide approach.

FACTORS PROMOTING ANTIBIOTIC RESISTANCE

Increased travel; availability of over-the-counter drugs; imprudent prescribing of antibiotics; poor patient compliance with antibiotics; decreasing funding of public health; day-care centers, long-term care facilities; use of antibiotics in agriculture.

UNNECESSARY USE OF ANTIBIOTICS IN THE UNITED STATES

Site	Unnecessary Use
Hospitals	25-45%
Community	20-50%
Farms	40-80%

(Office of Technology Assessment, 1995)

FACTORS PROMOTING ANTIBIOTIC RESISTANCE IN HOSPITALS

Greater severity of illness in hospitalized patients; increasing proportion of immunocompromised patients; intense device use; increased use of antimicrobial prophylaxis; empiric poly-antimicrobial therapy; high antimicrobial usage/geographic area/unit time; infections at sites with large bacterial inocula and poor antibiotic penetration (e.g., respiratory tract and wound infections); deficiencies in infection control practices; decreased funding for infection control activities. (McGowan JE:

JK-Practitioner 7(4);2000: 302 - 307

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Bull NY Acad Med 1987;63:253-268)

ANTIMICROBIAL USAGE AND RESISTANCE – Evidence for a Causal Relationship

Changes in antimicrobial usage are paralleled by changes in the prevalence of resistance; resistance is more prevalent in nosocomial than in community-acquired bacterial strains; development of resistance during antimicrobial therapy. (Schlaus DM: Infect Control Hosp Epidemiol 1987; 18:278-291)

DEVELOPMENT OF RESISTANCE DURING ANTIMICROBIAL THERAPY

Review of 173 clinical studies involving more than 14,000 patients and 225 treatment regimens; resistance occurred in six percent of all infections; emergent resistance was significantly more common in ICU patients ($p < 0.0001$) and patients receiving mechanical ventilation ($p = 0.0003$); higher rates of resistance associated with lower respiratory tract infections, cystic fibrosis, acute osteomyelitis (tend to recur, sites of poor antibiotic penetration); higher rates with Ps. Aeruginosa, Serratia sp. Enterobacter. (Fish DN et al: Pharmacotherapy 1995; 15:279-291)

OTHER ISSUES

In most hospitals, antibiotics comprise 30% of the hospital budget; antibiotics are a major cause of adverse drug complications; ex., C difficili; 50% of antibiotics prescribed are inappropriate.

ENVIRONMENTAL ISSUES – Water/Food

Water Supply

Several well-publicized outbreaks of acute gastroenteritis due to Cryptosporidium, a one-celled tiny parasite, have been reported in the USA. The Cryptosporidium oocysts are resistant to disinfection by chlorine - boiling kills them. A few examples:

Rural Carrol County with a population of 64,900 suffered 13,000 cases of *Cryptosporidiosis* in one month. Between 1991-1992, 34 outbreaks of disease associated with drinking water were reported to federal agencies.

April 1993, 400,000 residents of Milwaukee, Wisconsin fell ill with *Cryptosporidium* – even had an impact on the outcome of an NBA game!

December 1993 this bug made its way into Washington, DC's water supply.

A citizens' action group estimated nearly one million Americans were falling ill annually due to water contamination, and 900 were dying as a result.

The other key microbes involved were Giardia, hepatitis A and Shigella.

Milk Sickens 11,000 in Japan

More than 11,000 people in western Japan were sickened by tainted milk in the country's largest case of food poisoning in decades, health officials said yesterday. (June 20, 2000)

Bacteria allowed to accumulate in a production-line valve caused the outbreak, which started last week when residents began suffering diarrhea and vomiting after drinking low-fat milk from Japan's largest maker of dairy products, Snow Brand Milk. By yesterday morning, 11,376 people had gotten sick and 165 required hospitalization, according to the Ministry of Health. Company president Tetsuro Ishikawa apologized and said he would resign September 30.

IMPORTED RASPBERRIES

Sometimes distant events show up in your backyard. Several outbreaks of "Cyclospora" infection caused by contamination of raspberries have been reported. Such outbreaks tend to occur in elite places such as cruise ships, clubs, etc., since the consumers of imported raspberries end to congregate in such areas.

NOSOCOMIAL SPREAD

An intern acquired *Cryptosporidium* from an AIDS patient. A few days later the intern's spouse got the Crypto gastroenteritis and studies showed 45% of all the intern's contacts had Cryptosporidium infection.

FOOD-BORNE INFECTIONS

- USA estimated 75 million illnesses/year, 325,000 hospitalizations, and 5,000 deaths.
- Increasing incidence of transmission of resistant organisms from animal food source – hamburgers, chicken to humans. Reasons:
  - 90% of all antibiotics used for food animals given in sub-therapeutic doses for growth promotion.
  - 40,000 – 50,000 pounds of antibiotics are used on fruit trees in the US each year (enough to treat 20 million people for one day).
    - In commercial fish farming, antibiotics are added in water.

In Europe, the emergence of Vancomycin-resistant Enterococci was associated with the use of Avoparcin as animal feed supplement.

In a landmark study in 1983, Michael Osterholm discovered that low-level livestock use of antibiotics led to mutant bacterial emergence and subsequent human disease. (Holmberg SD et al: New England Journal of

Medicine 1984, 311:617-22.)

SALMONELLA NEWPORT FOOD POISONING

Outbreak in Minnesota, South Dakota and North Dakota in 1983 traced to herd which had been fed antibiotic-laced feed at suboptimal levels leading to emergence of Salmonella resistance which eventually led to the outbreak. (Jukes TH: New England Journal of Medicine 1984, 311:1698-99)

E. COLI OUTBREAKS

One of the clearest and most troubling examples of animal/human cross species transmission.

1982 E. Coli 0157:H7 – Causes dangerous hemorrhages of colon, bowel and kidneys of human beings of all ages. Produces Shigella-like toxins.

1991 Outbreak of E. Coli 0157:H7 from local apple cider in Massachusetts. Cider made from apples plucked from trees that were fertilized with livestock manure. Manure was excreta of 0157:H7 infected animals.

January 1993 500 people in Washington State became seriously ill after eating hamburgers prepared in 93 Jack-in-the-Box fast-food restaurants. Several died – culprit: E.Coli, source: cattle. (Deresinki S: Infectious Diseases Alert 1993, 12:81-84.)

The unregulated use of antibiotics in livestock continues in an unregulated manner.

CHICKEN AS A SOURCE OF INFECTION

In the USA chickens are grown in factories. Salmonella and Campylobacteria are normal inhabitants. Due to crowded conditions, the normal fecal flora gets on the feather follicles and contaminates the skin. Up to 10% have Salmonella, and 95% Campylobacter when studied on supermarket shelves.

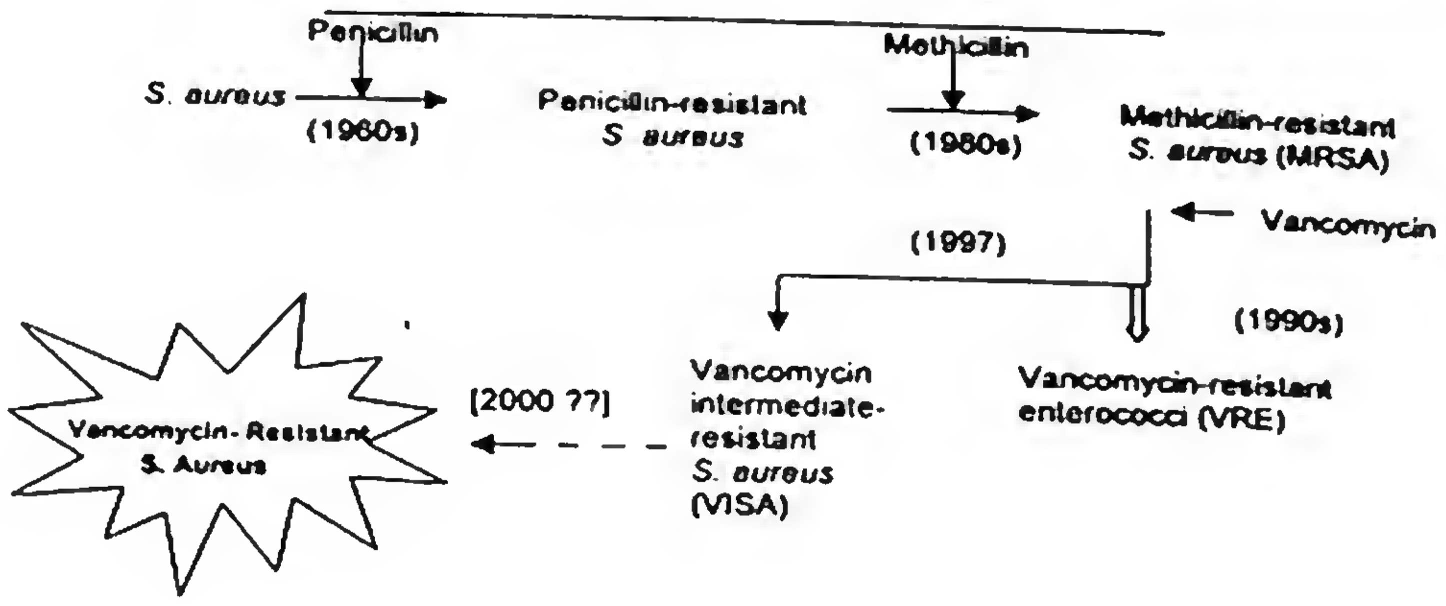
In 1995 Ciprofloxacin was approved for therapeutic use in animals. Entire flocks get treated via water supply. Results of resistance of Campylobacter to Ciprofloxacin were predictable:

1992	Ciprofloxacin resistance 1%
1995	Ciprofloxacin approved for usage.
1997	12% resistance
1998	13% resistance
1999	21% of Campylobacter are resistant to Ciprofloxacin

Infection with resistant strains have longer duration of illness.

Of interest is the majority of Guillan Barre Syndrome patients are related to prior Campylobacter infection, perhaps 1:1,000 infection. There are approximately 2-4 million cases of Campylobacter/year, thus the economic impact of Guillan Barre complication is huge.

EVOLUTION OF DRUG RESISTANCE IN S. AUREUS


Penicillin
S. aureus
(1960s)
Penicillin-resistant S. aureus
Methicillin
(1980s)
Methicillin-resistant S. aureus (MRSA)
Vancomycin
(1997)
(1990s)
Vancomycin-Resistant S. Aureus
[2000 ??]
Vancomycin intermediate-resistant S. aureus (VISA)
Vancomycin-resistant enterococci (VRE)

STAPHYLOCOCCUS AUREUS

- ☐ Appear on gram stain as gram-positive cocci in clusters.
- ☐ Causes disease via:
  - direct invasion
  - metastatic seeding
  - toxin production (food poisoning, toxic shock syndrome, scalded skin syndrome).
- ☐ Most common nosocomial pathogen overall (13%).
- ☐ Most common cause of surgical wound infection (20%).
- ☐ Most common cause of nosocomial pneumonia (19%).

CONTRIBUTIONS OF S. AUREUS TO DISEASE BURDEN

INFECTION	% DUE TO S. AUREUS
Bacteremia	15
Endocarditis	30
Surgical Site	20
Osteomyelitis	50
Septic Arthritis – Adults	55

(Rubin RJ et al. Emerging Infection Diseases 1999, 5:9-17.)

GLYCOPEPTIDE INTERMEDIATE S. AUREUS – Common Features

- Prior infection with MRSA
- Repeated and prolonged Vancomycin therapy
- Dialysis
- Poor clinical response to Vancomycin
- Susceptible to alternative agents

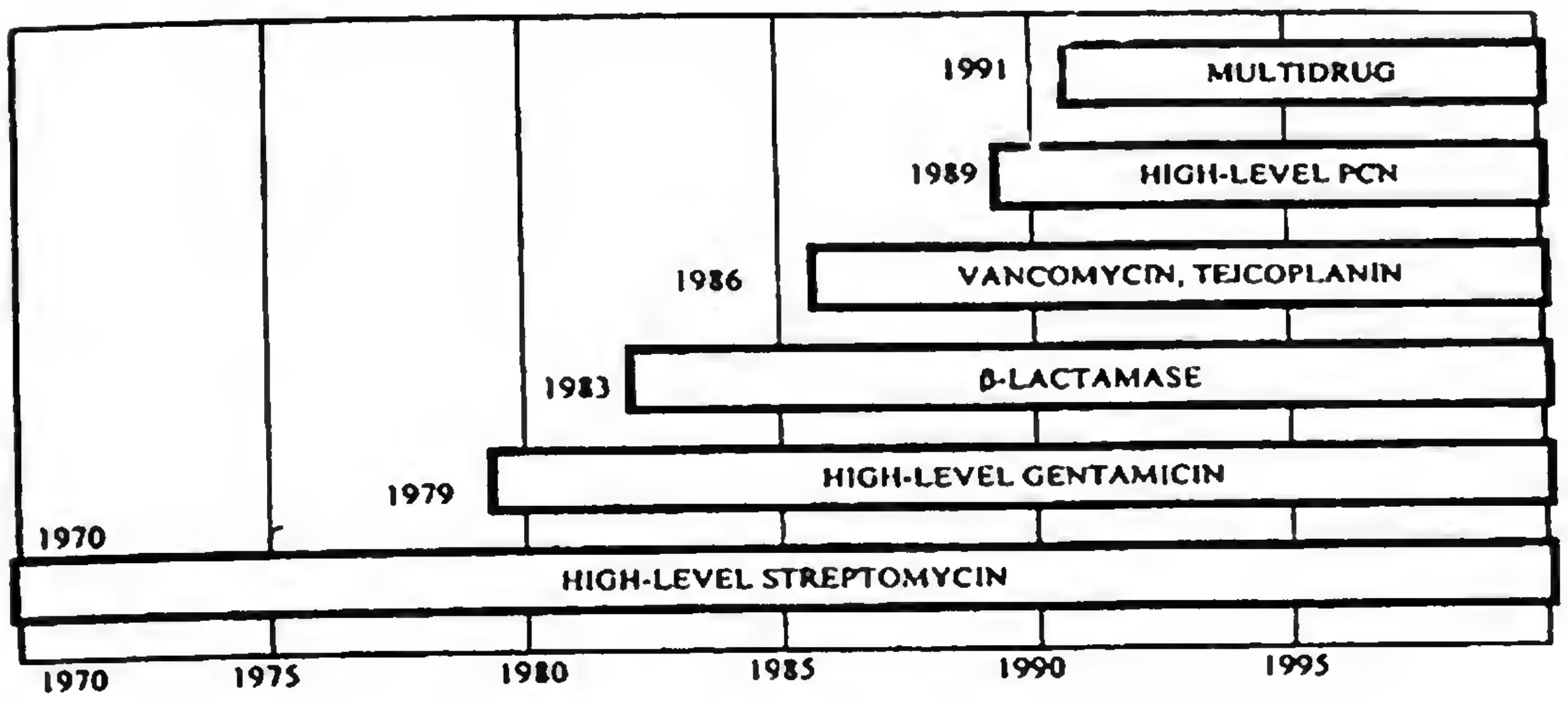
(Smith T et al: New England Journal of Medicine 1999; 340:493-501)

Using PCR genetic fingerprinting, investigators in New York discovered that all 470 MRSA strains descended from a strain that first emerged in Cairo, Egypt in 1961. A decade later these strains were seen planet wide. (Kreiswirth B et al: Science 1993; 259:227-30)

ENTEROCOCCI:
Important Nosocomial Pathogens

Normal flora of the GI tract
Antimicrobial resistance allows survival in an environment with heavy use of antibiotics
Survive heat and desiccation; can survive in the environment for prolonged periods of time
Healthcare workers provide the potential for spread
Over 20% of hospital isolates are resistant to Vancomycin
40% of patients with VRE bacteremia die

ENTEROCOCCI:
Acquired Resistance



RISK FACTORS FOR VRE COLONIZATION AND INFECTION

- Extended hospital stay
- Extended ICU stay
- Prior nosocomial infection
- Proximity to other patients with VRE
- Severe illness
- Hematologic malignancy
- Mucositis
- Nurse caring for another VRE patient
- Neutropenia
- Liver transplantation
- Antimicrobials: Vancomycin, third-generation Cephalosporins, Ciprofloxacin, Anti-anaerobic drugs

Inside American hospitals the emergence of super-enterococci was facilitated by practices that allowed the organisms to instantly spread from one susceptible human to another: electronic thermometers, catheters and surgical instruments, intravenous lines, mechanical ventilation and overuse of Cephalosporin-type antibiotics. (Livornese LL, Jr et al: Annals of Internal Medicine 1992; 117:112-116. Pallares R et al: Archives of Internal Medicine 1993; 153:1581-86.)

HERPES VIRUS

By 1981 the U.S. genital herpes epidemic had reached crisis proportion. The arrival of Acyclovir, which could prevent latent herpes viruses from resurfacing to produce genital disease, cold sores, shingles, and a variety of other diseases, was a terrific success. Its arrival was hailed as a revolution similar to the arrival of penicillin four decades earlier. (Saral R: New England Journal of Medicine 1981; 305:63-67. Strauss SE: New England Journal of Medicine 1984; 310:1545-50.)

The enthusiasm and excitement was short-lived as resistant strains began to emerge, and serious herpes encephalitis relapses in patients following cessation of Acyclovir use were being reported. (Rothman AL et al: Journal of the American Medical Association 1988; 259:1056-57.)

By 1989 virulent Acyclovir-resistant mutants began to appear in AIDS patients. (Erlich KS et al: New England Journal of Medicine 1989; 320:293-96. Whitley RJ et al: New England Journal of Medicine 1992; 327:782-89.)

Predictably, resistance to other antivirals – Ganciclovir and Foscarnet – also began to emerge.

MALARIA

"More than ten percent of all admissions and outpatient visits are from malaria. In terms of death, it is quite high and it is apparent that malaria is much more severe now than before." (Dr. Wen Kilama, Director General of Tanzania's National Institute for Medical Research – 1986.)

In 1976 the first case of chloroquine-resistant Plasmodium falciparum parasites had emerged in Tanzania. By 1986 most of the nation's malaria was resistant to the world's most effective treatment.

The large percentage (more than 80%) of malaria cases occur in Africa. Up to one-million African children died each year of the disease. There has been a resurgence of malaria in Brazil and other countries.

By 1990 chloroquine resistance was the rule rather than the exception in most malarial regions of Africa, and the lethal form of cerebral malaria began to emerge in increasing numbers with increasing mortality. The associated economic costs were estimated to be $1.8 billion. (Garret Laurie: The Coming Plague, Chapter 13, pages 441-444. Publisher, Farrar, Starr and Giroux, New York, 1994)

Isolated reports of resistance to Mefloquine are also emerging.

SOLUTIONS AND RECOMMENDATIONS

Environmental Issues

The usage of antibiotics for growth promotion to animals needs to be tightly regulated. Europe has made some headway in this regard, particularly in Scandinavian countries.

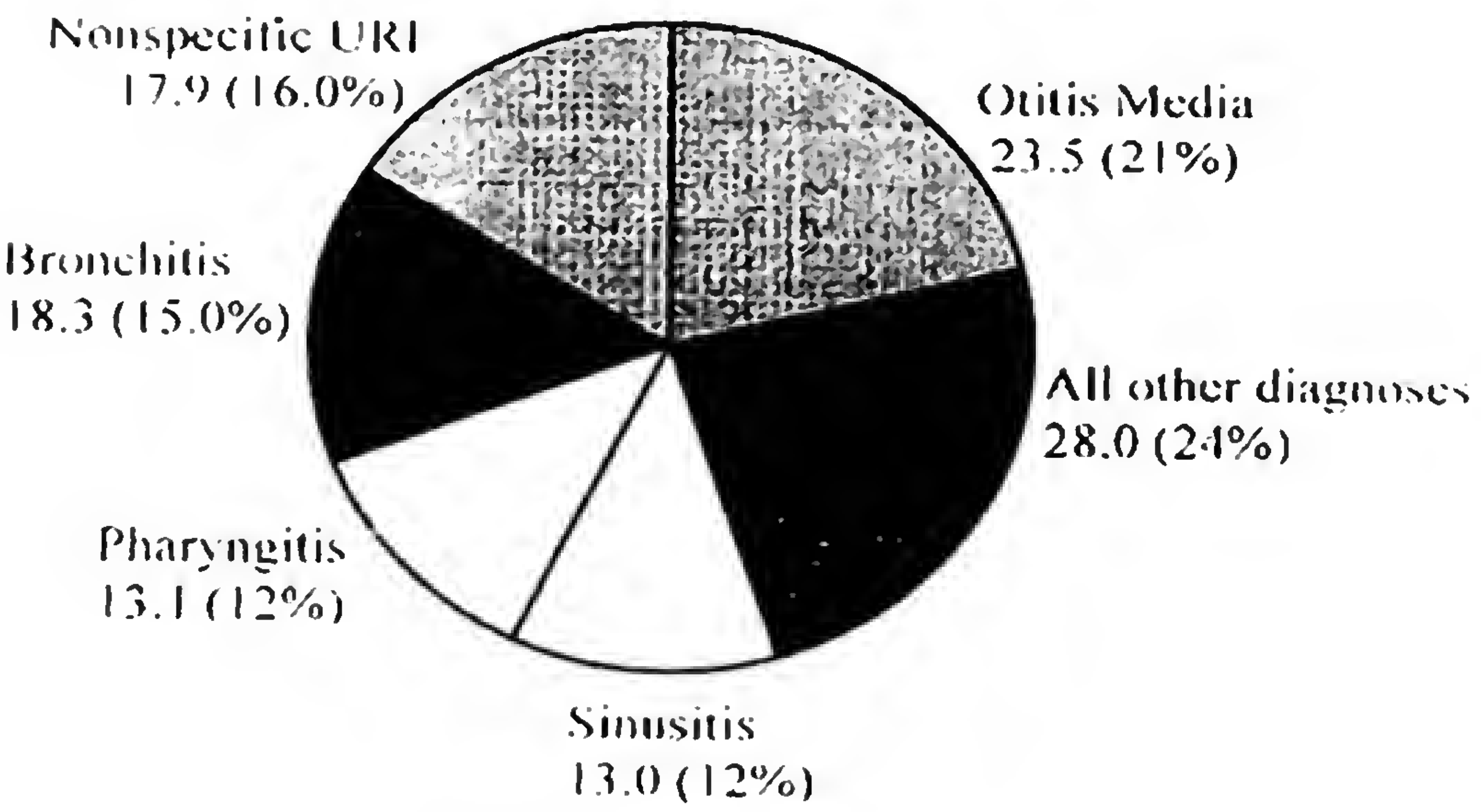
In Iceland and Hungary, reduced penicillin usage was associated with reduced strept pneumonia resistance.

Physicians' Role

The emerging antibiotic resistance is mediated by transference of genetic elements driven by antibiotic pressure in hospitals, usage by physicians, in particular in outpatient set-ups, and nosocomial spread within hospitals.

OUTPATIENT ANTIBIOTIC COURSES (IN MILLIONS) PRESCRIBED FOR COMMON DIAGNOSES BY U.S. PHYSICIANS IN 1992

JAMA 1995; 273:214-9



LEADING AMBULATORY CARE DIAGNOSES ACCOUNTING FOR ANTIBIOTIC PRESCRIPTIONS FOR ADULTS IN THE U.S.

JAMA 1997; 78:901-4

	DIAGNOSIS (ICD-9-CM Code)	OFFICE VISITS (In 1000's)	ANTIBIOTIC PRESCRIPTIONS (In 1000's)
Sinusitis	(461, 473)	13,369	7494
Bronchitis	(466, 490)	10,235	6752
URI	(460, 465)	11,033	5842
Pharyngitis	(462)	7,412	5634
UTI	(590, 595, 599)	4,858	2798
Otitis Media	(381.0, 381.3, 381.4, 382.0, 382.9)	4,226	2003

OTHER ISSUES

- ▲ 18% of parents give antibiotics before seeing doctors.
- ▲ Patients demand antibiotics.
- ▲ In some cultures, patients prefer injections to oral pills. 43% of doctors in practice more than 15 years change antibiotics while 29% of recent graduates change them.
- ▲ Direct marketing to patients by pharmaceuticals will have an adverse impact.
- ▲ Over-the-counter use of antibiotics is common in Asia and Africa.

ANTIBIOTIC PRESCRIBING FOR ADULTS WITH COLDS, UPPER RESPIRATORY TRACT INFECTIONS, AND BRONCHITIS BY AMBULATORY CARE PHYSICIANS

JAMA 1997, 78:901-4

Conclusion: Although antibiotics have little or no benefit for colds, upper respiratory tract infections, or bronchitis, these conditions account for a sizable proportion of total antibiotic prescriptions for adults by office-based physicians in the United States. Overuse of antibiotics is widespread across geographic areas, medical specialties, and payment sources. Therefore, effective strategies for changing prescribing behavior for these conditions will need to be broad based.

CONTROLLING ANTIMICROBIAL RESISTANCE IN HOSPITAL PATIENTS

Four broad strategies with twelve concrete steps.

A. Prevent Infection
   1. Vaccinate – influenza vaccine, S. Pneumoniae.
   2. Catheter – "Do I need this catheter today?" Get it out unless absolutely essential.

B. Eradicate Infection As Soon As Possible
   3. Diagnose the infection.
      Diagnose the pathogen.

Diagnose antimicrobial susceptibility.
Get some cultures.

4. Treat to cure!
    - Optimize regimen, dose, duration.
    - Monitor response.

C. Use Antimicrobials Wisely

5. Accept help – no one knows everything! Seek and accept input.
6. Know your antibiotics.
7. Target the pathogen.
8. Say "no" to Vanco.
9. Don't treat contaminants.
10. Quit when you are ahead.

D. Prevent Transmission

11. Isolate infection at source.
12. Proper hand hygiene.

In conclusion, it's clear that:

- Emerging antibiotic resistance is a major health issue worldwide.
- Bacteria, viruses, parasites are all affected by this.
- The prolific use of antibiotics in the promotion of growth in animals creates an environment for the emergence of resistant bacteria which are transmitted from animals to humans.
- Some parasites – Cryptosporidium – survive in a standard, well-chlorinated water supply.
- A large percentage of prescribed antibiotics in the developed world are used inappropriately.
- In a hospital setting, a well-outlined strategy, including a) infection prevention, b) eradicating infection, c) using antibiotics wisely, and d) preventing transmission will help reduce the incidence of antibiotic resistance.
- A concerted, coordinated effort by policymakers, consumers, pharmaceutical producers, physicians, and others are needed to have an impact on this serious health issue.
- Visit virtual annual session of ACP/ASIM to get summary reports of the antibiotic resistance and other themes. (www.acponline.org/vas2000)

FDI AWARD

Dr.Bashir Ahmad, MDS Assistant Professor ,Oral and Maxillofacial Surgery , Govt.Dental College,Srinagar bagged the award in the *Oral &Dental Research Category* of the FDI's "Top Ten Advances in Dentistry" competition.

Dr.Bashir from India was declared winner at the FDI's General Assembly in Mexico. In all 56 countries had participated in the Ccompetition.The Runners Up included:- Dr.Robert Morris (USA),Dr.Vincent Conforti (USA),Dr.Harold Levenstein (South Africa)Dr.Olga Lopez Soto (Columbia),Prof.B Srinivasan (India),Dr.Santiago Moncayo (Columbia),Dr.John Helm (Sweden),Prof. Dragostav Djukanovic (Serbia), Dr.Margareta Helauder (Sweden),Dr.Poonam Jain (USA).

As a winner Dr.Ahmad is entitled to an all expenses paid trip to the FDI's Centenary Congress In Paris,which includes a free flight,free accomodation and free Congress registration.The dates of the Congress are 29th.November -2nd. December 2000.

ANAESTHESIA IN DENTISTRY

Mohd Amin Wani M.D.; Javid Iqbal Naqishbandi M.D., D.N.B., Mutahira Abeeda Wahid M.S.; Safa Abida M.B.B.S.

1. ANAESTHESIA IN DENTISTRY:

can be subdivided into following types

a) Dental chair Anaesthesia
   e.g. Simple tooth extractions
b) Day-Case Anaesthesia
   e.g. 1. Straight forward extraction of molars
   2. Minor oral surgery
c) Inpatient Anaesthesia
   e.g. 1. More complicated extractions
   2. Oral surgical procedures
d) Sedation techniques with monitored anesthesia care.

GENERAL DENTAL COUNSIL AND DEPARTMENT OF HEALTH RECOMMENDATIONS (1991)

1. a) Avoid General anesthesia as far as possible.
   b) Anesthesia to be given by a trained Anaesthesiologist only.
   c) At any place where dental anesthesia is required, similar standards should be met in the form of
      - Premises
      - Personnel
      - Equipment
2. Sedation to be preferred over General anaesthesia and to be given by a trained person.
3. Resuscitation programme should include:
   a) Teaching
   b) Training
   c) Assessment of the trainees
   d) Facilities made available for cardiopulmonary resuscitation.

DENTAL CHAIR ANAESTHESIA (GA FOR OUTPATIENT DENTAL EXTRACTIONS)

Pre-requisites:

1. Healthy patients (American society of Anaesthetists class I & Class II)
2. Dental practitioner should have medical knowledge
3. In patients between 4-10 years rule out upper respiratoryn infection
4. Surgical procedure should be of short duration & protoperative pain should be manageable on domiciliary basis.
5. Social Circumstances
   a) Adult responsible attendant should be accompany the patient.
   b) Domestic arrangements to nurse the patient should be dappropriate

PROPER EQUIPMENT FOR ANAESTHESIA ALSO THE NEEDING

a) 100% O^2 (fast flow)
b) Nitrous oxide
c) Vapouriser
d) Anaesthesia Circuits
e) Resuscitation apparatus
f) Suction unit
g) Chair with head down tilt even with power failure
h) Resuscitation team should include
   Anesthesist
   Dentist
   Dental Nurse

MINIMUM MANDATORY MONITORING:

1. ECG
2. Pulse oximetry
3. Non-invasive Blood pressure
4. Carbon dioxide monitoring

INDICATION FOR GENERAL ANAESTHESIA:

1. Children
2. Dental abscess (Because local anaesthetics are ineffective)
3. Un-Cooperative patient
   a) Mental impairment
   b) Physical disability

POTENTIAL PRE-OPERATIVE PROBLEMS:

1. Poorly prepsared Patient
2. Children with upper respiratory infection
3. Difficult airway
4. Inadequate facilities

PER OPERATIVE PROBLEMS:

1. Un-cooperative child-difficult induction.
2. Airway problems
   a) Irritant gas
   b) Gag
   c) Pack
   d) Bleeding
   e) Broken tooth
3. Cardaic arythmias.

POSTOPERATIVE PROBLEMS

a) Immediate
- Hypoxemia
- Airway problems
- Vomiting

b) Delayed
- Bleeding
- Pain and Swelling
- Nausea and Vomiting

POSTOPERATIVE ANALGESIA:

NSAIDS a) Oral
b) Rectal (Under GA)

DISCHARGE FITNESS:

1. Alert
2. Oriented
3. Stand and Walk

DAY-CASE ANAESTHESIA

☐ Formal hospital admission after proper preanaesthesia check up done only.
☐ ASA I and II patient to be admitted
☐ Patient to be discharged same day.
☐ Indications.
- Limited dental extractions (Wisdom tooth)
- Minor surgical procedures (LASER)

☐ Nasotracheal or orotracheal intubation
☐ Throat pack to be kept with the tail protruding out
☐ Left lateral tilt with head down position before extubation.

ANALGESIA:

1. Opioids
2. NSAIDS.
3. Steroids (as anti inflamatory)
4. Local Nerve Blocks
   (Not all 4 quadrants)

DISCHARGE CRITERIA:

1. Good pain Control
2. No Bleeding
3. Fully oriented with time, space and person.
4. Accompanied by a responsible adult
5. Written and verbal instructions to be given to the patient.
6. Contact Number of the concerned doctor to be given to the patient.

IN-PATIENTS ANAESTHESIA

1. Needed for more invasive procedures like
   a) All 4 wisdom teeth extractions
   b) Surgery on gums and jaws
2. Pre-anaesthesia check up is a must becuase of possible limited jaw movement which might necessitate Blind nasotracheal or fibroptic endotracheal intubation.

SEDATION TECHNIQUES

DOH Definition of Sedation:

A carefully conrolled technique in which a single intravenous drug or a combination of Oxygen and nitrous oxide is used to reinforce hypnotic suggesion and reassurance in a way which allows dental treatment to be performed with minimal physiological and psychological stress but which allows verbal contact with the patient to be maintained at all times.

Techniques:

1. Intravenous Sedation
   a No anxiety
   b) Drowsy but co-operative and easily arousable
   c) Midazolam (1mg/Kg)/Local anaesthesia
      Dreams of sexual nature misunderstanding should be avoided by keeping a nurse near the female patient.
   d) Monitor continously
   e) Accompanied by a responsible attendant
   f) Rest for 24 hrs.
2. Inhalational Sedation.
   (Relative analgesia) For Needle - Phobia
   a) Oxygen + Nitrous oxide (Nasal mask)
   b) Local anaesthesia.
   c) Rest for 24 hours.

DENTAL ANAESTHESIA IN SPECIAL SITUATIONS:

Haemophilia:

- Laryngeal Mask Airway/Endotrachel tube
- Preoperative prepatation to build coagulogram
- Intra muscular Injections to be avoided.
- Intra venous Injections to be preffered
- Synthetic Vasopression and Tromboxane-A (Pre-post operatively)
- Metaculous Haemostasis

Young Patients for IIIrd Molar Extraction:

- Ventricular Premature contractions is a possibility

Cardiac patients for Dental extraction:

a) Antibiotics for infective endocarditis prophylaxis
b) Local anaesthesia to be prefferd

EMERGENCY SURGERY:

Rule out:

- Polytrauma
- Hypovolumia
- Airway Compromise —may need:
  a) Fibro optic bronchoscopy
  b) Tracheostomy
  c) Antiemetics

Mentally Handicapped patients:

Increased incidence of Dental Caries

Rule out:

- Congenital Cardiac defects
- Chronic lung Disease
- Possible drung intake

EMERGENCY DRUGS IN DENTAL PRACTICE:

1. Oxygen
2. Adrenaline (1, in 10,000)
3. Lignocaine 1%
4. Atropine
5. Calcium chloride injections
6. Sod. bicarbonate
7. Aminophylline
8. Salbutamol inhaler
9. Chlorpheneramine

MORALITY:

- Low compared to other Surgeries
- Due to
  a) Trained Anaesthetist
  b) Sedation & LOcal anaesthesia preffered over general anaesthesia.
- Need to decrease Generalk anaesthesia will be ensured by:
  a) Public Education
  b) Preventive Dentistry

ROLE OF DENTIST IN ANAESTHESIA:

☐ Preparation of Mouth Guard for ease of endotracheal intubation in partially edentulous patients.

OPACIFIED LEFT HEMITHORAX WITH CAVITARY DISEASE OF THE RIGHT LUNG

Musarat Shareeff, M.D.; Yasser Bhat M.D.; Faroque A.Khan M.B., M.A.C.P.

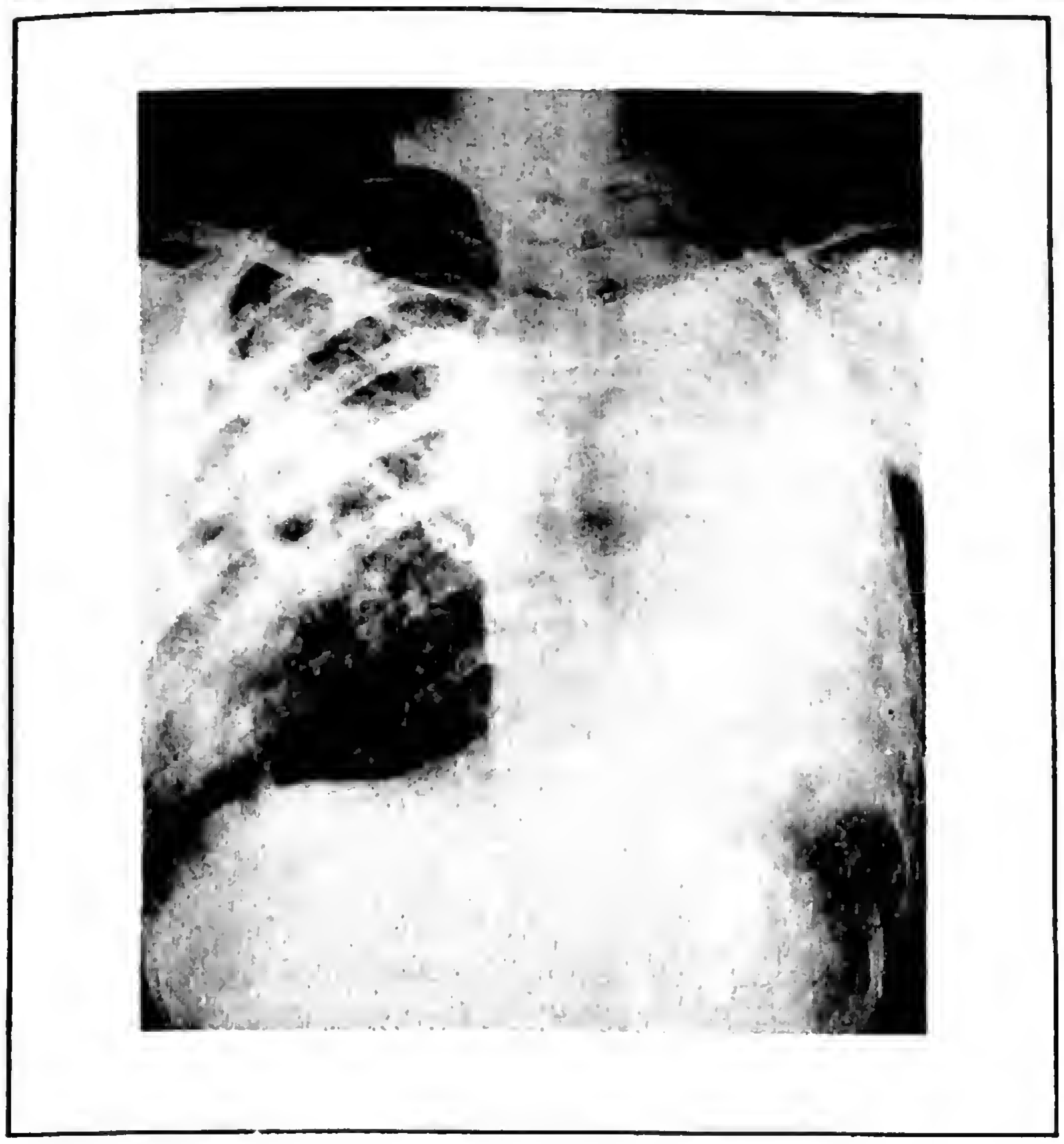


Fig.I

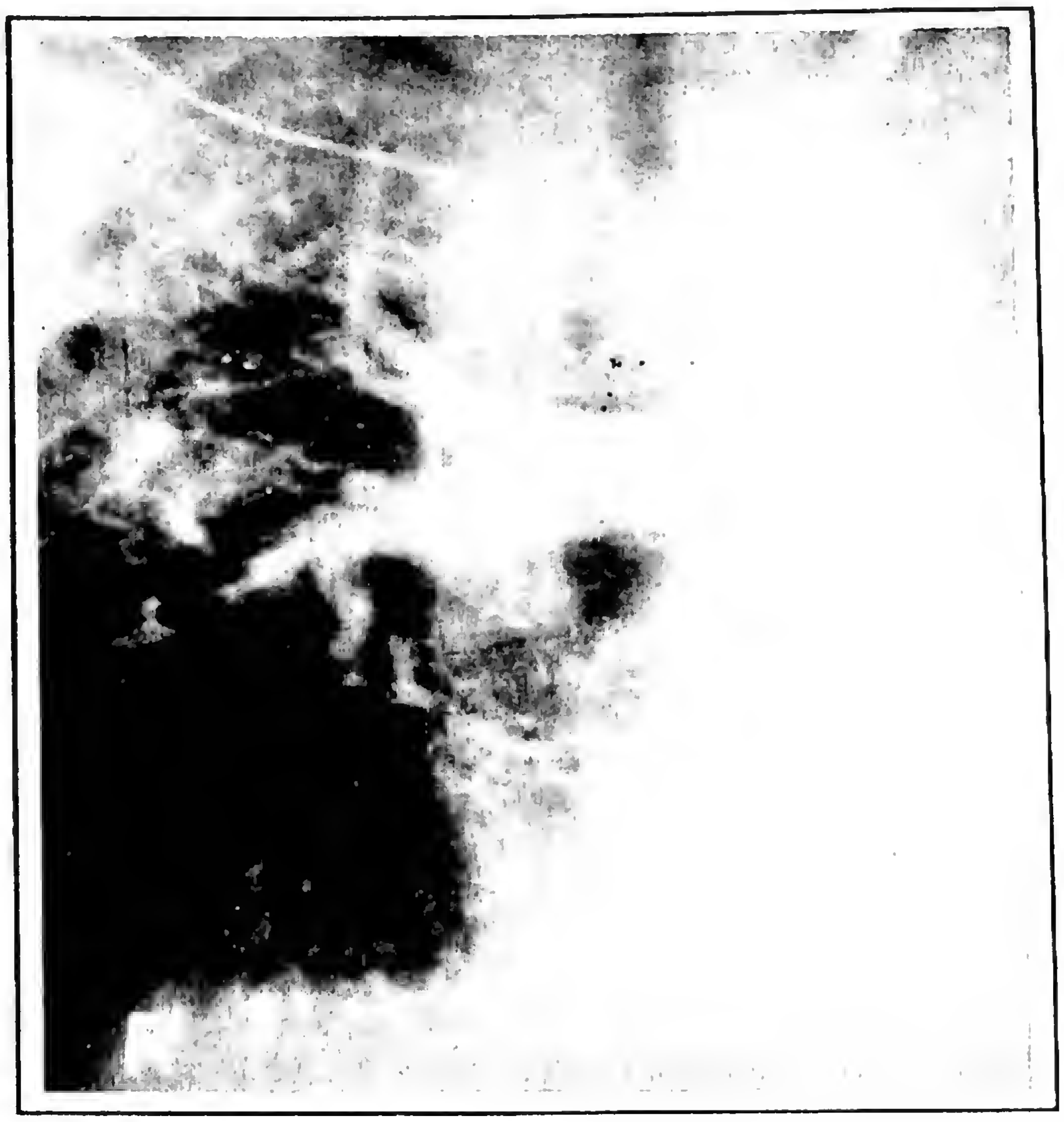


Fig.II

This 39 years old Puerto Rican woman was admitted to the hospital complaining of hemoptysis of two days' duration. She described recurrent attacks of cough with expectorations for six weeks, associated with dyspnea. Following a routine medical evaluation at the age of 19, she was told that her lung was "completely hazy" on chest radiograph. She then received antituberculous chemotherapy for two years. There was no history of chest surgery or trauma.

On physical examination, she was in no distress, and she had normal vital signs. Clubbing of the fingers was present. Both hemithoraces were of equal size, but there was diminished expansion, dullness to percussion, and diminished breath sounds over the left chest. Rales were present over the posterior portion of the right upper lobe. The apex beat was in the fifth left intercostal space in the anterior axillary line. There was no cardiac murmur. Routine laboratory evaluation was normal. An intermediate PPD test was positive. Figure 1 represents the chest roentgenogram on admission.

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What is the diagnosis?

Diagnosis: Left Pulmonary Agenesis; Tuberculosis of the Right Lung

Figure I' shows cavitary disease in the right lung and complete opacification and displacement of the heart and mediastinum into the left hemithorax. Compensatory over-expansion of the right lung with herniation to the left side is also noted.

The diagnosis of pulmonary tuberculosis was confirmed when sputum cultures grew acid-fast bacilli. To further elaborate the status of the left lung, bronchoscopy was carried out. This showed the left main bronchus ending in a blind pouch. Biopsy of the pouch did not reveal any abnormality. Pulmonary angiogram showed absence of the left main pulmonary artery and its branches (Figure II). The total absence of vessels on the left side along with the bronchoscopic findings of lack of bronchial development confirms the diagnosis of agenesis of the left lung.[1,2,5,]

Agenesis of the lung was first described by De Pozze in 1673 at the autopsy of an adult woman. The etiology is unknown but a few causes such as genetic defects teratogenic factors, vitamin A deficiency and viruses have been postulated[1,4]. The association with congenital defects in other organs points to generalized teratogenic etiology,[4,2] however, Schober et al have described a case of pulmonary agenesis in partial trisomy 2q and 21p[5] and Mardini et al reported parental consanguinity in all four patients and hence suggests in autosomal mode of inheritance.[6].

In more than 50% of the cases it is associated with congenital defects of other organ systems like the cardiac, genitourinary, gastrointestinal and skeletal systems[1,2,5,6]. Pulmonary agenesis does not give rise to symptoms unless complicated by bronchopulmonary disease. In most cases, patients present with repeated chest infections. The time on onset of symptoms are remarkably variable ranging from a few minutes after birth to adulthood. Presenting symptoms are tachypnea with or without cyanosis, lower respiratory tract infections, bronchitis, asthmatic bronchitis or pneumonia.[1] There is no definite evidence that pulmonary arterial hypertension develops in patients with unilateral agenesis of lungs, however, Capuani A et al, have reported the incidence to be 29% in patients with unilateral agenesis while in patients with additional left to right shunt the incidence is 88%.[2,7]

Diagnosis is often suggested by the chest radiography. Computed tomography, echocardiography, bronchoscopy and pulmonary angiography are needed to confirm the diagnosis.[1,2,5,] About half of all reported cases die either at birth or within the first five years of life. There appears to be no predilection of either sex or either lung[1,2]. Cases that survive childhood are relatively asymptomatic, the survival depending upon the presence or absence of associated cardiovascular abnormalities. Patients with left lung agenesis survive longer than those with right lung defects, probably due to more severe mediastinal and cardiac shift[1], the difference in the degree of mediastinal shift perhaps related to the volume loss, the right lung with three lobes representing 55% of the total lung volume and the left lung with the two lobes representing 45% of the total volume.

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A SECONDARY LIVER EXTENDING ON TO SKIN SURFACE AS PARIETAL WALL ABSCESS IN A PATIENT WITH UNKNOWN PRIMARY

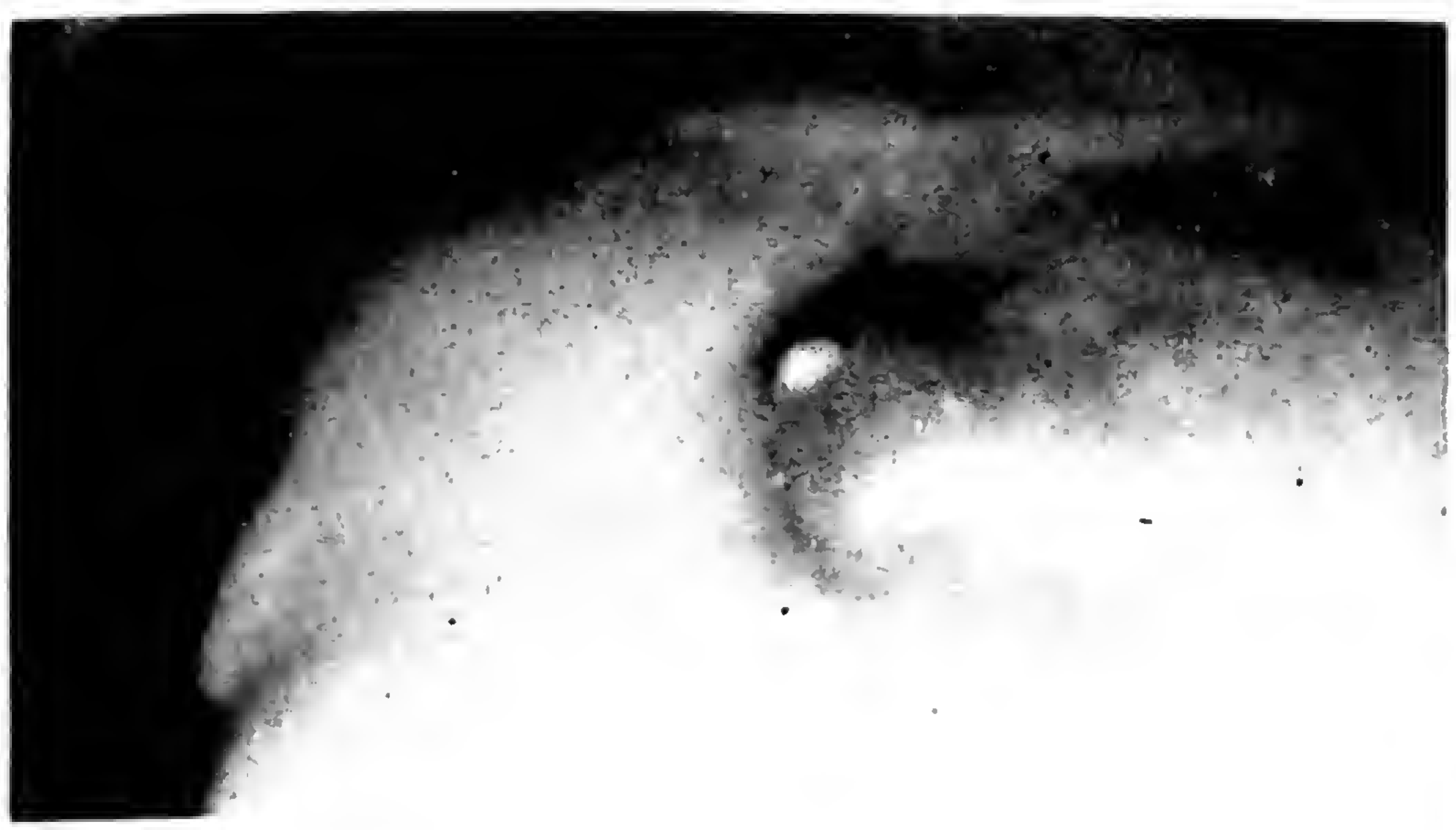

Fig. 1. Patient with inflammatory smelling over right hypochondium lower chest wall and epigastrium. It also reveals a pus point about to rupture.

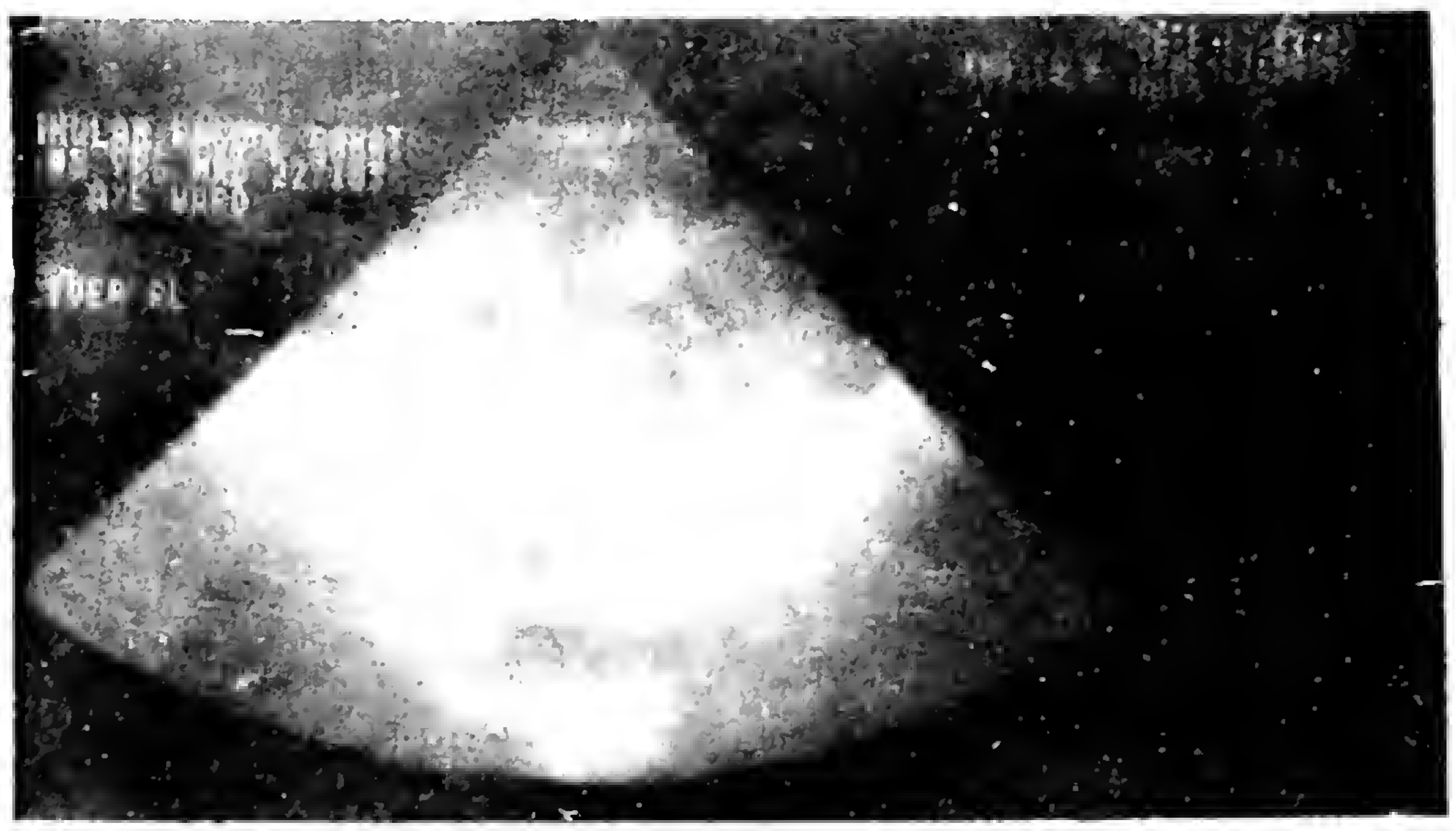

Fig. 2. Ultrasonograph revealing lerge secondary in the liver with central necrosis.

A 48 year old male presented to the Emergency Department with pain (abdomen) over right hypochondrium of 1 month duration. His ultrasound abdomen revealed a secondary in right lobe of liver measuring 5.0x6.1cm. His detailed investigations failed to locate the primary. Meanwhile ultrasound guided aspiration (USGA) revealed cytological features of an undifferentiated malignant epithelial tumour. Patient went home and again reported to emergency department after one month with pain and swelling over abdomen. Local examination revealed an inflammatory swelling over right hypochondrium extending on to chest wall and epigastrium 10x15cm in size and arising from the liver. It was cystic in consistency and revealed a pus point. Ultrasonography revealed a necrotic large secondary in liver extending on to skin surface. About 100ml of pus was drained from the site.

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GHULAM RASOOL MEMORIAL AWARDS

The suggestion for initiating an Annual Ghulam Rasool Memorial Awards was made during the inaugural lecture held in memory of the late pioneer surgeon of Kashmir, Ghulam Rasool, during the international conference on *Recent Advances in Medicine* held in Srinagar, Kashmir from August 21-23, 1999. This award was made possible with the support of the *Arfa and Fafoque Khan (AFK) Foundation*. The highlights of the lecture were published in *the J&K Practitioner* Vol. 6, No. 4, October-December 1999.

In response to the announcement of this award, eight essays were received, focused on health care in Kashmir. Six were submitted by medical students of Government Medical College, and two by postgraduate trainees. These essays provided an excellent overview of the current health status in Kashmir. The topics ranged from an analysis of the current situation, impact of past decades' turbulence on health care with deterioratioin of infrastructure, collapse of rural health care, overload of urban centers, marked increase in trauma cases, and psychiatric disorders. The exodus of key teachers and specialists made the situation even worse. They are briefly summarized below.

Yasser Yousuf Wani

2nd MBBS, GMC: *Current Medical Scenario in Kashmir: An Introspection*. In a well-outlined format the health problems emanating since 1989 are reviewed, listing six reasons for the problem, nine reasons for the continuation of these problems, and fourteen suggested remedies with one reference.

Sajid Muzaffar

3rd year, GMC: *Orthopedic Care in Kashmir*. This essay gives an historic reivew of the orthopedic problems in the valley, with a focus on the Bone and Joint (B&J) Hospital. Statistics with appropriate tables regarding staffing at B&J, with a lack of state-of-the-art diagnostic facilities, are present.

M. Mohsin Chisti

3rd MBBS, GMC: *Health Care in Kashmir*. This well-written essay outlines the types of health care in Kashmir, the impact of the decade-old crisis resulting in the collapse of rural health care with severe overcrowding on the urban health centers.

Irfan Jehangir

Prefinal, GMC: *Health Care in Kashmir*. In this essay, after outlining the set-up for health care delivery, the author emphasizes the need for upgrading care at the pimary level in local districts, which will have an impact on the care provided in tertiary centers. The author uses the success of polio eradication as an example of the success of primary care.

IInd Ghulam Rasool Memorial Lecture being delivered by Dr. Farooque A. Khan

Fiaz Ahmad Baba

3rd year, GMC: *How to Modify Health Care in Kashmir*. In this well-though-out essay, the author provides concrete recommendations for improving health care in Kashmir. He suggests several cirriculum changes at undergraduate and postgraduate levels. he recommends monitoring and quality control of medical shops, and increased resources towards the prevalent neuropsychiatric problems. Finally, the author recognizes the need for education of the people via the media and laments on the increasing environmental pollution in the valley with consequent health consequences.

Sameena Muzaffar

Prefinal, GMC: *Leprosy Care in Kashmir*. In this essay the author provides statistics regarding leprosy cases in the valley, the format under which they are followed, and the difficulties encountered in providing care in remote rural areas - particularly due to continued social stigma attached to this disease.

Dr. Javid Ahmad Shah

PG Student, SKIMS: *Metal Health in Kashmir*. This essay described, in some detail, the present fast-increasing, stress-related psychiatric problems and the lack of facilities for providing care to these patients.

The author states there has been over a twenty-fold increase in psychiatric disorders, and urges quick remedial measures, in particular, due to increasing substance abuse.

Dr. Rumana Makhdoomi

Kashmiri Patients: Innocent or Ignorant? In this provocative essay, the author cites the examples of four patients who, to say the least, received very poor care and virtually no information regarding their disease from their doctors. The author laments on the alarming rate of breakdown of basic professional ethics amongst physicains, and reinforces the basic need for recognizing patients' rights, particularly amongst the younger generation of physicians.

When we announced the *Ghulam Rasool Memorial Awards*, we were not sure what type of response would be elicited. Needless to say, we were pleasantly surprised and, in our view all eight submitters were winners. However, while the content of all eight essays was excellent, the essays of Yasser Wani and Fiaz Baba were judged best amongst students entries, and Dr. Rumana Makhdoomis the best among postgraduate students, based on layout, presentation, and style. These awards were presented in August 2000 at the conclusion of the second *Ghulam Rasool Lecture* titled *How To Make An Effective Presentation* by Dr. Faroque Khan.

We look forward to receiving submissions for the year 2001 *Ghulam Rasool Awards*, the deadline for which is April 30, 2001, to be sent to 95 Karol Place, Jericho, NY 11753-1306. U.S.A.

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MARCH TOWARDS MORALITY. (IS KASHMIRI MEDICAL COMMUNITY READY?)

Kashmir is known as a paradise on earth. It has witnessed a serve political turmoil in last one decade. Breakdown of law and order has undoubtedly affected all walks of human life. Health care system was no exception. Medical education as well as medical care showed a drift in its standards. Doctors as well as patients were frustrated.

However God always sends rescue to those who deserve it. The first important change was the publication of first medical journal from this part of the world. The credit goes to all the senior doctors of the valley led by Professor G.M. Malik. It will be an important landmark in the history of Medicine in Kashmir. This journal has awakened and stimulated scientific thinking in the medical community of Kashmir and has therefore been an important and marvelous initial kick in proper direction. I am greatly impressed by the number of articles appearing in this journal from Kashmir valley. Dr. Malik and his team needs a sincere and honest appreciation for his contribution and he will be remembered forever in Kashmir Medical history.

Organizing an international conference on Recent Advances in Medicine on 21-23 August 1999 by professor G.Q. Allaqaband and Dr. Kamili had an important effect of breaking the ice for the first time in ten years history of tension and turmoil. Non-resident Kashmiri (NRK) doctors especially those from USA were instrumental in organizing this conference. Organizing as yet another international conference on 29-30 July 2000 in less than a year was a breath-taking event. It was held in collaboration with British Kashmiri Doctors Association (BKDA), in Hotel Grand Palace (Old Oberoi Palace). Overlooking the crystal clear water of Dal Lake surrounded by green clad hills added an emotional and psychologically Kashmiri touch to this gigantic get-together of medical community. I have witnessed for the first time in ten years that doctors bursting into laughter after laughter as if they were all born afresh. I even overheard some of the senior and retired physicians telling each other that this gathering has added ten years to their life and that there was no need for a coronary angiogram in near future. From Kashmir to U.S.A. and U.K. to Saudi Arabia, medicine of all regions was discussed. This gathering stimulated the interpersonal, social, cultural as well as the academic thinking of Kashmiri physicians. It was simply marvelous and organizers need sincere and special thanks for all their efforts and a full co-operation in future.

However that is not enough. We need to update and upgrade our professional standards further. Many of the areas need to be identified and improved. One of the common observations both by the patients as well as by many doctors has been the falling standard of morality in the profession. Empathy is lacking in many of the doctors. Malpractice and unscientific management is witnessed quite frequently. Sometimes even witnessed in tertiary cares centres. Lack of harmony among the staff and even sometimes within the faculty members of some of the units is so prominent that patient's feel dejected and run away from the hospitals. Doctors patient relationship is either considered as master servant relationship or at times exploited to morally defaming ends. Patient care has therefore suffered and deteriorated. The problem is really serious and something needs to be done. In a conversation of senior professors during the July 29-30th, 2000 conference, opinion differed regarding the main reasons responsible for deteriorating patient care. Lack of managerial skills among the present day physicians, economic crunch in the state and red-tapism in non-technical beurocracy, all had their own advocates.

Although these things are not going to change overnight but efforts should be started as early as possible. Medical profession in Kashmir needs to be directed properly so that it will be prevented from further degeneration. One of the ways, it could be done is to form a loose association of all the physicians of Kashmir. A body of all retired professors and senior physicians of repute will crown this association. Experience and talent of these technocrats could be thus effectively utilized in guiding the younger physicians. Such purely profession organisation could work only to maintain highest level of moral and ethical standards within the profession. They can advice on ways and means of resolving conflicts within the medical community and can also advise on discipline and empathy. Even clinical practice can be watched and scrutinized and concerned physicians advised whenever and wherever they deviate. Private sector is also rapidly establishing itself in the valley. And so are the fears amongst the public that this noble profession might be converted into a trade where consumers are totally blind, thus there is a scope for exploitation. A professional body could effectively check such a tendency.

It is also very much clear that most of our doctors are not getting proper training in doctor-patient relationship, communication skills and human psychology and dyadic relationship. Similarly they are also trained to think in a purely organic model, where as they need to be trained to think in a psycho-socio-organic way which means a considerable shift from the existing practice. This could be included in the curriculum of the medical graduates and postgraduates. Similarly topics on these subjects can be discussed in detail in all the academic meetings.

Given proper guidance Kashmiri talent can be channeled and projected at the international level. But by for the most important would be an honest appreciation by our own patients and their complete belief on the profession which is right now in a very shaky an unstable state. I hope that our seniors will come forward to take up this challenge and will lead this profession to higher levels of excellence during this century.

Good, better, best, never let it rest,
Till good becomes better, and better becomes best.

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NATIONAL AIDS AWARENESS CAMPAIGN — A REPORT

National AIDS awareness campaign was started by J&K AIDS prevention & control society with active collaboration of Dept. of SPM Govt. Medical College Sgr.. Aids –a dreadful disease, which has already crossed the epidemiological mark of 1% in the country, has already started appearing in J&K with estimated figures of 14000 as per NACO 1998 estimates. In order to make doctors aware NACO in association with J&KAPCS flew in resource persons from New Delhi which included—DR. A.S. Rathore-joint Director NACO, Dr.R.S.Misra –HOD Dermatology & Director Regional STD Training Canter Safdurjung Hospital Delhi, Dr Geeta Mehta HOD Microbiology Lady Harding Medical College Delhi, Dr. Manoroma Singh HOD Gyne/Obstetrics RMLH Hospital Delhi. Dr. B.B Rewari physician specialists RML Hospital & Nita Mawar Asst. Director National AIDS Research Institute (NARI) Pune. These resources persons trained about 43 core group doctors from various specialties of SMHS & Associated Hospitals, SKIMS & Govt Dental College Sgr. They included Dept of Medicine ,Gyne /Obstetrics, Dermatology ,Social & Preventive Medicine ,Pharmacology, pathology & Microbiology, Govt. Medical College Sgr. Dept of Community Medicine SKIMS, Medical Superintendents of SMHS,CD Hospital, LD Hospital, Pediatric Hospital &Orthopedics Hospital. These core group doctors were given extensive training in handling, diagnosis, counseling, treatment & other aspects of AIDS. This core group traing was held on 20,21,22 june 2000. The core group trained the doctors from field and from Medical Education department. An extensive three days workshops were and are being held in which doctors participated whole heartedly first such group was trained on 20-22nd of July, 2000, in which about fifteen doctors from Directorate of Health Services and about fourteen doctors from Medical Education Department.

The second similar batch was trained from 10-12th of August, 00, in which twenty more doctors deputed by the Director, Health Services and ten doctors from Medical Education department participated. The third batch of doctors from field as well as from Medical Education department was trained from 5-7th September,00 (ten doctors deputed by the Director, Health Services, Kashmir). One more batch i.e; fourth batch of doctors (mostly specialists) was trained on 25-27th September,00, in which twenty doctors/specialists from Associated Hospitals and field practice area of Govt. Medical College, Srinagar were imparted training.

A further follow up of two more batches of Medical Officers/Sepecialists are being trained in the near future exlusively for field doctos i.e; from Directorate of Health Services.

Over and above, training programmes for para-medical staff from the field practice area of Govt. Medical College, Srinagar and its associated Hospitals are being organized very soon. It is expected a universal AIDS hotline with a number 1096 will also be available for telecounselling purpose of general public in the department of Social Preventive Medicine, Govt. Medical College, Srinagar. In near future. Training of religious scvholars especially MOLIVIS is also being proposed in neart future.

All this was possible with active support of Mr. Ashok Jaitley chief secretary J&K Govt.,Mr. H.L. Kadulbaju Commisinor Secretary Medical & Health Education Dept., Mr. Ashok Parimar Prooject Director J&KAPCS., Prof. A.Rouf Principal Govt Medical College Sgr chief coordinator, Dr. Muneer A. Massodi HOD SPM & co-cordinator. There dedicated services will lead to fruitful outcome of this awareness programme with decrease in incidence of AIDS cases .in conculsion we would like to stress on following slogans:

KNOW AIDS FOR NO AIDS
DONOT CONDEMN AIDS CONDOM IT.

Dr.Rafiq
PG, Deptt. of SPM, GMC Srinagar

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CONFER
1999

1. Inaugural ceremony of the International Conference: Recent Advances in Medicine and Update, held on August 21-22, 1999 in progress. From L to R. Dr. G. M. Malik, Dr. S. N. A. Shah, Dr. Phoola Koul, Dr. Farooq Abdullah (CM J&K), Dr Mustafa Kamal (Health Minister J&K)

2. Some of the Delegates attending the Conference. (Medicine Update Aug 21-22, 1999) From Lto R: Dr. G. M. Malik, Dr. M. Bukhari, Dr. M. A. Kamili, Dr. F. A. Khan, Dr. Arifa Khan, Dr. Naria Khuroo, Dr. M. S. Khuroo, Dr. Saima Qazi, Dr. Tanveer Mir, Mr. S. Fazili and Dr. A. R. Mir

3. World AIDS day organisied by IMA & GMC in Srinagar at Medical College Auditorium (Dec. 1, 1999), (Dr. Misger, making a speach) (Seated from L to R: Dr. A Ahad, Dr. G. M. Malik, Dr. Ashiq Hussain, Dr. Mir Nazir)

4. A view of the audience (AIDS Day Dec 1, 1999) Seen seated in front from L to R: Dr. G. Q. Allaqaband, Dr. S. N. Ahmad Shah and Dr. B. M. Bhan.

DOCTOR'S DAY ON 1st. JULY

5. Doctors Day Celebration (July Ist. 1999) on the dias from Lto R: Dr. Mir Nazir, Dr. G. M. Malik, Dr. S. N. Ahmad Shah, Dr. Phoola Koul.

6. Principal GMC Srinagar Dr. Phoola Koul awarding a cash prize and certificate of merit to the best outgoing graduate, to Dr. Farah (Courtesy JK-Practitioner

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NOZCON 2000
Annual Conference
INTERNATIONAL COLLEGE OF SURGEONS
INDIAN SECTION NORTH ZONE
in collaboration with

The annual conference of Surgeons Indian section-NZ was held in collaboration with Regional Surgeons Association Jammu on 7-8 April 2000 at GMC, Jammu (J&K). Post Conference workshops on VATS and Endo (Lapro) Gynae. were held on 9-4-2000. More than 250 delegates attended. Guest speakers included Dr. Naresh Trehan (Raj Nanda Orator 2000) Dr. Ahmad Abdul Hai (Patna). Dr. P. K. Dave Director AIIMS. Dr. H. S. Bhanushali (VATS surgeon Mumbai). Dr. Narender J Pandya, Plastic Reconstruction Surgeon, Mumbai. Dr. P. N. Joshi (Colorectal Surgeon Mumbai) Dr. J. D. Wig (P. G. I.) Dr. Vijay Arora (Lap Surgeon Delhi) Dr. Anil Sharma (Lap Surgeon Delhi) Dr. Shakti Gupta (AIIMS) Dr. N. K. Pandey (Escorts Hospital Faridabad)

From Lt-Rt. Dr Chrungoo (Org. Secretary), Dr. Pathania President JK Branch, Dr. Goswami Principal GMC Jammu, Dr. N K Panday Vice President
Dr. Farooq Abdullah (CM), Mr. Mian Altaf Hon. Health Minister, Dr. N. J. Pandaya President
Mr. Ajay Shatroo Hon. Minister, Chowdary M Ramzan Hon Minister

"International Conference on Recent Advances in Medicine — An Update"
Kashmir India

This conference was arranged by the Government Medical College (GMC) in Srinagar. Kashmir and was endorsed by the Medical Counsil of India. It was held at the scenic convention centre of Dal Lake Srinagar August 1999. Over 500 registrants participated in the meeting and the topics reviewed ranged from pulmonary diseases, cardiovascular diseases, women's health, imaging, gastroenterology, infectious diseases and geriatrics. The faculty is comprised of the medical school faculty from Kashmir and ten faculty members from the USA, most of whom were alumni of GMC. In addition to the scientific sessions, there was an excellent cultural programme prepared by medical students.

The meeting provided an opportunity to review medical issues from Eastern and Western perspective. Based on the evaluations, feedback and attendance, the meeting was very successful. Dr. G. M. Malik from Kashmir and Farooque A Khan, MB, MACP from the USA were the co-directors of the conference.

This report appeard in the ACP - ASIM International Newletter (Vol.3 Winter 2000, Edition Page 3.)

L.-R. **Dr. Samia Qazi (USA)**, **Dr. Tanvir Mir (Regent ACP, NY, USA)**, **Dr. Kamili (Jt. Org. Secy)**, **Dr. Rouf Mir Nephrologist (USA)**
Prof. M.S. Khuroo (Gastroenterologist) (KSA), **Prof. F.A. Khan (Regent ACP, NY, USA)**, **Dr. Parveez Mir Pulmonologist (USA)**